

100
CASE HISTORIES
IN CLINICAL MEDICINE
For MRCP (PART 1)

IMPORTANT NOTICE

Medicine is an everchanging science.
Efforts have been made to
include current concepts and therapies.
Readers are therefore
advised to consult
a standard textbook of medicine
for more details.

100 CASE HISTORIES IN CLINICAL MEDICINE for MRCP (Part 1)

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JAYPEE BROTHERS

MEDICAL PUBLISHERS (P) LTD.

New Delhi

Published by

Jitendar P Vij

Jaypee Brothers Medical Publishers (P) Ltd

EMCA House, 23/23B Ansari Road, Daryaganj

New Delhi 110 002, India

Phones: 23272143, 23272703, 23282021, 23245672, 23245683

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100 Case Histories in Medicine

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First Edition: 2001

Second Edition: **2004**

ISBN 81-8061-307-0

Typeset at JPBMP typesetting unit

Printed at

*This book is dedicated
to my
Parents
who taught me
how to read and write*

Foreword

I was privileged to be asked to write a foreword to this book published by a very practical and excellent clinical educator. It was a source of pride for me as he was my talented pupil with most distinguished college record and later on a very successful physician. It was a great pleasure to read the book as it deals with the practical problems faced in general wards of hospitals in Pakistan.

A manual to be carried in the pocket of every medical student. Being myself a life-long teaching physician in a clinical setting, I find this book a good contribution to the subject of clinical medicine giving a good coverage to different sections of internal medicine. The presentation is simple, readable, accurate and with a sound scientific foundation. One feels pleasure and satisfaction after going through it. This book is an extra help to those doctors who are preparing for FCPS (Medicine), MRCP (UK) and MD (Medicine) examinations.

I have no doubt that this book work will receive respect, admiration and success it rightly deserves from undergraduate, postgraduate medical students and family practitioners.

Prof M Akhtar Khan

Retired Professor of Medicine
and

Principal, King Edward Medical College
Lahore, Pakistan

Preface

Medical science is a very vast field and is expanding every day. It is extremely difficult to keep abreast the knowledge, as lots of advancements have been made in this field every moment and the concepts keep on changing perpetually. However, a medical doctor should at least be aware of common medical problems which he could face in his professional career. These problems may present individually or as multisystem disorders. Basic working knowledge and clinical skills are required to analyze these problems methodically and reach to a diagnosis and then plan appropriate management.

This book is an effort to pick up the “brains” by exercising problem solving. The set up is very simple. A brief history and important clues on clinical examination along with investigations are provided. Few important investigations are intentionally omitted and are asked in questions. In a few histories, the ECG or X-ray is shown and the reader is expected to interpret those to reach a diagnosis. In this book SI units have been used.

The lay out is in the form of chapters which are named system-wise and the diagnosis of case histories are labelled as such. If a reader is interested to read the cases related to, for example, cardiology, then the reader can go through that chapter and so on. An attempt has been made to improve important questions related to the text and current concepts are also discussed. This book will not only help problem solving in day-to-day life of medical doctors but will also serve as a purpose for preparing them for their postgraduate examination in medicine, e.g. FCPS, MRCP and others.

All these cases were actually recorded and collected by the author over the last three years and a lot of effort was put in to formulate in the form of a book. However, in such a small book the information contained cannot be comprehensive and it may not be a substitute for a textbook either. Therefore, the candidates should consult one of the standard textbooks in internal medicine to expand their knowledge.

The size of this book is such that it can be kept in the pocket so that the reader, whenever gets time should sit, have a cup of tea,

relax and go through it. I also firmly believe that the clinical skills of history taking and examination make the main pillar of good medical practice and most of the cases depend upon clinical presentation and examination. Although every effort has been made to write this book in a simple way, but if there are any suggestions for improvement, I would be more than happy to welcome them.

I would like to thank my colleagues for encouraging me to write this book. I am highly indebted to Dr Asif Kamal FRCP (Lond), FRCP (Edin), and Dr Avinash Mithal FRCP (Lond), FRCP (Edin), both Consultant Physicians at Lincoln County Hospitals, UK, for encouraging me, to write this book and for useful suggestions and allowing me to follow their footsteps in academics all the time during my stay in the United Kingdom and even to date. I am grateful to my wife, Shahina Farrukh, my daughters Saliha and Zunaira and my son Aizad who extended their full support in writing this book.

The second edition is completely revised after the sale of one thousand copies in less than one year. In this edition, current informations on various topics have been included. A conversion table along with normal values is added in the end of this book.

Lastly I shall welcome constructive and healthy criticisms and suggestions to improve this book, so that they should be included in the future editions.

Farrukh Iqbal

Acknowledgements

I am personally thankful to Prof Anwar A Khan (Gastroenterology), Chairman and Dean of Shaikh Zayed Postgraduate Medical Institute Prof Abdul Hayee (Haematology), Prof Muhammad Asim Khan from the USA (Rheumatology), Prof Saulat Siddique (Cardiology), Dr Nazim H Bokhari (Pulmonology) and Dr Nadir Zafar Khan (Neurology) all from Shaikh Zayed Postgraduate Medical Institute, Lahore for reading the relative chapters of the script and giving their valuable suggestions. I am also grateful to Prof Tahir Shafi, Professor of Nephrology and Ex-Chairman and Dean of Shaikh Zayed Postgraduate Medical Institute for being very kind and affectionate and of course to Prof Zafar Iqbal, Professor of Medicine for his encouragement and co-operation in writing this book. It would not be fair if I do not mention about a number of my students who actually made this book practically possible by continuously hammering me to get it published. I am indebted to Mr M Shahzad Mughal from the Institute of Education and Research, University of the Punjab for composing the manuscript. I am also thankful to all my other colleagues who have helped me in all ways.

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Rheumatic Heart Disease

BRIEF HISTORY

An 18-year-old girl was admitted through out-patient department with six hours history of severe left sided chest pain. For the last four months, she had increasing shortness of breath and fatigue on exertion with swelling of her ankles. During the last four hours of her chest pain, her breathlessness had worsened. There was no history of haemoptysis. She had mild unproductive cough for the last three months. The chest pain was described as sharp with no radiation and was worse on deep breathing. She had been given frusemide 40 mg daily for her swollen legs and had also been started on digoxin 0.25 mg once a day a week before her admission. Her doctor had given her pethidine 50 mg parenterally before sending her to the hospital, but this had failed to control her pain. She had no known drug allergies. She could remember having frequent sore throats as a child, but there was no clear history of joint pains. One of her brothers, however, had a heart condition and had been treated with medicines for a long time.

IMPORTANT CLUES ON CLINICAL EXAMINATION

On examination, she was very dyspnoeic and had central cyanosis. She was apyrexial. JVP was raised by 4 cm. There was moderate pitting oedema over her both legs. Her throat was normal. Blood pressure was 120/70 mm Hg. There was no clubbing or lymphadenopathy. Clinically she was euthyroid. Her pulse was 110 per minute and irregularly irregular. Peripheral pulses were palpable. Apex beat was tapping in character and she had a left parasternal heave. The first heart sound was loud and she had a rough, rumbling, mid-diastolic murmur localized to the apex.

2 Cardiology

Opening snap followed closely on the second heart sound. She had bilateral basal crackles with dullness and diminished air entry at her left base. There was no pleural rub. Liver was 4 cm enlarged, smooth and tender. There was no splenomegaly or ascites. Fundi were normal and there were no localizing neurological signs.

INVESTIGATIONS

The following results of the initial investigations were available:

Hb:	12.8 g/dl (normocytic normochromic)	Blood sugar	6.6 mmol/l (118 mg/dl)
		Blood urea	6.8 mmol/l (41 mg/dl)
		Creatinine:	110 umol/l (1.2 mg/dl)
WCC:	9.2 × 10 ⁹ /l P:76% L:20% M:2%E:2%	Urine:	trace of protein
		ECG:	confirmed atrial
Platelets :	310 × 10 ⁹ /l		fibrillation, there were no ischaemic changes.
ESR:	60 mm in 1st hour		
Sodium:	134 mmol/l		
Potassium :	3.6 mmol/l		
Bicarbonate:	24 mmol/l		
Chloride:	99 mmol/l		

QUESTIONS

- Q.1. What is the most likely diagnosis and what complication has occurred?
- Q.2. What further four investigations will help the diagnosis?
- Q.3. Give six important steps in the management of this patient.
- Q.4. What criteria is applied to this disease?

ANSWERS

A.1. The most likely diagnosis in this young girl with four months history of increasing fatigue, shortness of breath, swelling of ankles with previous history of repeated sore throats and characteristic findings of mitral stenosis, is rheumatic heart disease. Sudden sharp pleuritic chest pain in a girl with mitral stenosis and atrial fibrillation strongly supports the diagnosis of pulmonary embolism. Systemic or pulmonary embolism is a common complication of atrial fibrillation. A pleural rub is not always present and may sometimes be difficult to detect in the presence of diffuse crackles and/or effusion.

- A.2.**
- i. Chest X-ray
 - ii. Ventilation-perfusion (V/Q) scan
 - iii. Echocardiography
 - iv. Pulmonary angiography.

- A.3.**
- i. Oxygen inhalation.
 - ii. Anti-coagulation (start with heparin).
 - iii. Control of pain. Strong analgesics.
 - iv. Digoxin to control atrial fibrillation.
 - v. Diuretics preferably given parenterally to dry up the lungs.
 - vi. Consider using thrombolytic therapy (streptokinase).

A.4. This includes major and minor criteria called Duckitt Jones's criteria.

The major criteria:

- i. Carditis
- ii. Polyarthrititis
- iii. Chorea (Sydenham's)
- iv. Erythema marginatum
- v. Subcutaneous nodules.

The minor criteria:

- i. Fever.
- ii. Arthralgia.
- iii. Raised ESR or positive C-reactive protein in high titres.
- iv. Prolonged P-R interval on ECG.

Two major and one minor or one major and two minor criteria are required to diagnose rheumatic fever.

2 C A S E

Left Atrial Myxoma

BRIEF HISTORY

A 35-year-old man presented to the cardiology outpatient with a history of fever, malaise and palpitations for the last four months. The fever was low grade and intermittent in character. On one occasion, he developed sudden pain in the left leg which became pale, cold and heavy. Two weeks prior to his recent visit to the hospital, he had a syncopal attack and recovered spontaneously. There was no history of chest pain but occasionally he had dyspnoea on exertion.

IMPORTANT CLUES ON CLINICAL EXAMINATION

On examination, he looked pale and a bit anxious. Temperature was 99.4°F. General physical examination was normal. Pulse was 96 per min, regular and good volume with all peripheral pulses palpable. BP was 130/85 mm Hg. First heart sound was split with accentuation of the pulmonic component of second heart sound and mid-diastolic murmur at mitral area. Chest examination revealed bilateral basal crackles. Abdominal and neurological systems were normal.

INVESTIGATIONS

Investigations included:

Hb:	9.8 g/dl (normocytic normochromic)	Blood sugar:	4.4 mmol/l (79 mg/dl)
		Blood urea:	8 mmol/l (48 mg/dl)
		Creatinine:	108 umol/l (1.2 mg/dl)
WCC:	$8.8 \times 10^9 / l$	Urine:	normal
	P:76% L:20%	ECG:	sinus rhythm, no ischaemic changes
	M:2%E:2%		

Contd...

Contd...

Platelets:	310 × 10 ⁹ /l		
ESR:	95 mm in 1st hour	Chest X-ray:	straightening of left border of heart which was normal in size.
Sodium	138 mmol/l		
Potassium:	4.2 mmol/l		
Bicarbonate:	26 mmol/l		
Chloride:	99 mmol/l		

QUESTIONS

- Q.1. What is the diagnosis?
- Q.2. What further investigations would you ask for?
- Q.3. What happens to the immuno-electrophoretic pattern in this condition?
- Q.4. Give a brief account about this condition.
- Q.5. What is the treatment?

ANSWERS

- A.1. In a person who had history of low grade fever, weight loss, occlusion of an artery (left lower limb), a syncopal attack and raised ESR point towards a diagnosis of left atrial myxoma. Presence of murmur makes it more probable.
- A.2. Echocardiogram is characteristic in this case. There is persistent uniform echogenicity behind the anterior mitral valve leaflet if the myxoma is protruding in the mitral valve area on M-mode while on two-dimensional view, the myxoma is visible in the left atrium.
- A.3. There is increase in IgG fraction of gamma globulins.
- A.4. Although these are rare primary tumours of the heart, but they are potentially curable. They occur most frequently in the atria, and left atrium is involved three times more than the right atrium. They may be unilateral or bilateral and are often pedunculated, while if they are present in the ventricles, they are sessile. The symptoms result from impediment to blood flow through the heart, embolization from the tumour in the systemic or pulmonary beds and generalised constitutional abnormalities. Left atrial myxomas mimic mitral stenosis or regurgitation and their sequelae, while right atrial myxoma presents as tricuspid stenosis.
- A.5. It is surgical resection of the tumour which results in complete cure, including relief of the constitutional symptoms. Because of the potential for recurrence, the endocardial attachment should be excised. Follow-up echocardiography is required afterwards.

3 C A S E

Infective Endocarditis

BRIEF HISTORY

A 60-year-old woman was admitted through the outpatient clinic with a four-month history of weight loss, loss of appetite and fever with rigors and night sweats. She also complained of increased breathlessness and tiny reddish lesions on the palms and pulp of the fingers which were painful. She also had some dragging sensation in the left hypochondrium. In the past, she was operated for mitral valve stenosis by valvotomy. She was a known hypertensive and diabetic.

IMPORTANT CLUES ON CLINICAL EXAMINATION

On examination, she looked pale and had a temperature of 100°F. She was clubbed and there were a few streaks in her nails. Pulse was 108 per minute regular, and all the pulses were palpable. Heart sounds were normal, but there was a pan-systolic murmur at mitral area which radiated towards left axilla. Chest was clear but abdominal examination revealed splenomegaly. Neurological examination was normal.

INVESTIGATIONS

Investigations included:

Hb:	8.4 g/dl (normocytic normochromic)	Urine:	traces of albumin and a few RBCs per high power field seen.
WBC:	16.6 × 10 ⁹ /l P:71% L:21% M:5% E:3%	Chest X-ray:	mitralization of the left border of heart with prominent

Contd...

8 Cardiology

Contd...

ESR:	95 mm in 1st hour	pulmonary blood vessels.
Sodium:	140 mmol/l	
Potassium:	4.3 mmol/l	
Bicarbonate:	25 mmol/l	
Chloride:	110 mmol/l	

QUESTIONS

- Q.1. What is the diagnosis?
- Q.2. What further investigations would you ask for?
- Q.3. What possible organisms are involved?
- Q.4. What do you know in reference to Libman Sacks?
- Q.5. What are the vasculitic lesions of this disorder?
- Q.6. What is the treatment?

ANSWERS

- A.1.** The history, examination and investigations lead to a diagnosis of infective endocarditis.
- A.2.** i. *Blood cultures*: At least four to six sets of blood culture are required, but one should be aware of special media for other organisms. At least 5 to 10 ml of blood should be withdrawn for each example.
 ii. *Echocardiogram*: To see any vegetations on the mitral valve.
- A.3.** i. *Streptococcus viridans* vii. *Brucella*
 ii. *Streptococcus faecalis* viii. *Listeria*
 iii. *Staphylococcus aureus* ix. *Candida*
 iv. *Pneumococcus* x. *Aspergillus*
 v. *Gonococcus* xi. *Coliform bacteria*
 vi. *Histoplasma* xii. *Coxiella burnetii*
- A.4.** These are non-infective vegetations which occur in systemic lupus erythematosus called Libman-Sacks endocarditis.
- A.5.** The vasculitic lesions include, Osler's nodes, which are tender subcutaneous nodules and are purplish or reddish. They classically occur on finger pulps. Janeway's lesions are large, erythematous, painful and tender maculopapular lesions which may develop on the palms or soles. Roth's spots are small, flame-shaped haemorrhages which are found in the retina and may also have a pale centre.
- A.6.** Mostly it is *streptococcus viridans* and, therefore benzyl penicillin is the treatment of choice which is supplemented with gentamycin for synergistic effect. The former should be given parenterally for four weeks, while the latter can be given for the first two weeks. Penicillinase resistant penicillin analogues should be used in cases due to penicillin-resistant organisms, e.g. methicillin, oxacillin, nafcillin, cephalosporins, etc. In patients who are allergic to penicillin, erythromycin, cephalosporins and vancomycin are alternative drugs.
 Fungal infections are treated with amphotericin B therapy. If bacterial endocarditis develops more than six weeks after the cessation of treatment, it usually is a new infection.

4 C A S E

WPW Syndrome

BRIEF HISTORY

A 27-year-old man presented to the accident and emergency department with a history of palpitations. He said that he had such palpitations quite often and on two occasions felt dizzy as well. There was no history of fever, chest pain, dyspnoea on exertion, undue intolerance to heat or weight loss. There was no past history of painful swollen joints during adolescent period. He was not a known hypertensive or diabetic. He smoked ten cigarettes a day.

IMPORTANT CLUES ON CLINICAL EXAMINATION

On examination, he looked well and in good health. Pulse was 90 per minute, good volume, regular, and all pulses were palpable. His JVP was not raised and heart sounds were normal. Blood pressure was 125/80 mmHg. His chest was clear. Abdominal and neurological examinations were normal.

INVESTIGATIONS

Investigations were as follows:

Hb:	15 g/dl (normocytic normochromic)	Chloride:	98 mmol/l
		Urine:	normal
WBC:	$7.9 \times 10^9/l$ P:75% L:20% M:3%E:2%	Chest X-ray:	normal
		ECG:	as shown in Figure 4.1
ESR:	04 mm in 1st hour	Echocardiogram:	normal
Platelets:	$290 \times 10^9/l$		
Sodium:	138 mmol/l		
Potassium:	4.8 mmol/l		
Bicarbonate:	24 mmol/l		

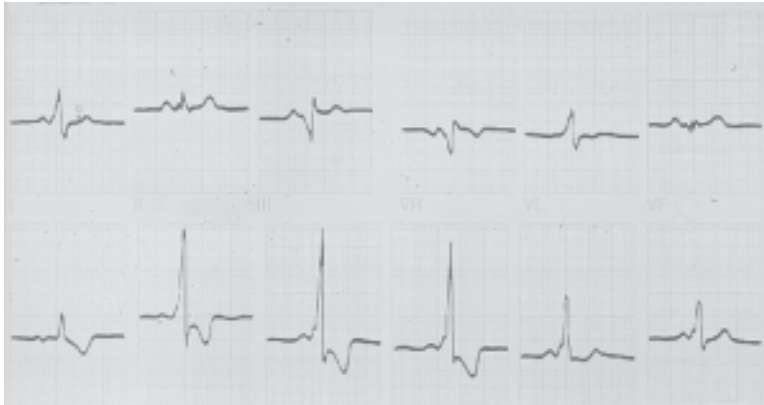


Fig. 4.1: Wolff-Parkinson-White syndrome

QUESTIONS

- Q.1.** What is the diagnosis in this case?
- Q.2.** What are the characteristic changes on ECG?
- Q.3.** Where is the abnormality?
- Q.4.** What is the treatment?
- Q.5.** What are the other associations of this condition?

ANSWERS

- A.1. With history of palpitations in a young man with no other systemic involvement and a clue on ECG favours a diagnosis of Wolff-Parkinson-White syndrome (WPW syndrome).
 - A.2. The P wave is normal, P-R interval is short (less than 0.12 sec) and there is a little slur (delta wave) on the ascending limb of QRS complex, which may be broad as well. There is a pronounced tendency for the occurrence of atrial tachyarrhythmias which may lead to ventricular tachyarrhythmia, e.g. ventricular tachycardia and ventricular fibrillation.
 - A.3. There are accessory conduction pathways from atria to ventricles bypassing the AV node. They are three in number namely—bundle of Kent, bundle of James and bundle of Mahaim. Short circuiting occurs and the patient gets tachyarrhythmias including supra-ventricular and ventricular tachycardia which can progress to ventricular fibrillation and death.
 - A.4. This may be medical and consists of those drugs which prolong refractory period of cardiac conduction tissue, e.g. amiodarone (Cordarone). For surgical treatment, electrophysiological study of the heart is important and tractectomy by cryosurgery is done. Radioablation may also be an option.
 - A.5. Pre-excitation syndrome is associated with Ebsteins and other cardiac anomalies, e.g. mitral valve prolapse, hypertrophic cardiomyopathy.
- NB:** WPW syndrome should be differentiated from LGL syndrome (Lown-Ganong-Levine syndrome) in which there is normal p-wave, short PR interval, short QS interval, but there is no delta-wave on the ascending limb of QRS complex.

5 C A S E

Acute Pericarditis

BRIEF HISTORY

A young man presented with chest pain which was retrosternal in origin. The pain was sharp, pricking in character and aggravated while lying down, but he got a little relief while sitting up. He gave history of an upper respiratory tract infection accompanied by fever about five days ago. He was a non-smoker. There was no history of trauma, hypertension or diabetes.

IMPORTANT CLUES ON CLINICAL EXAMINATION

On examination, he looked anxious. Temperature was 102°F. Pulse was 110 per minute, regular, good volume and all pulses were palpable. Cardiovascular system revealed normal heart sounds, but there was some scratchy noise over the precordium. Both lungs were clear on auscultation. Abdominal and neurological examinations were normal.

INVESTIGATIONS

Investigations included:

Hb	15 g/dl (normocytic normochromic)	Potassium:	4.8 mmol/l
		Bicarbonate:	24 mmol/l
		Chloride:	98 mmol/l
WBC:	$7.5 \times 10^9/l$ P:60% L:35% M:3%E:2%	Chest X-ray:	lungs clear and heart size normal
Platelets:	$250 \times 10^9/l$	ECG:	as shown in Figure 5.1
ESR:	38 mm in 1st hour		
Sodium:	138 mmol/l		

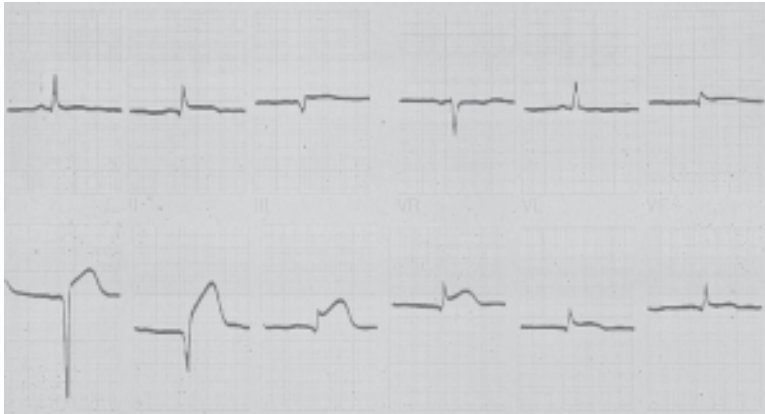


Fig. 5.1: Pericarditis

QUESTIONS

- Q.1.** What is the diagnosis?
- Q.2.** Give a few causes of this disease.
- Q.3.** What is Bornholm's myalgia or devils grip?
- Q.4.** What are the complications of your final diagnosis?
- Q.5.** What is the treatment?

ANSWERS

- A.1.** In a young man, a history of fever, upper respiratory tract infection, retrosternal pain which is posture related with classical ECG changes point to a diagnosis of acute pericarditis.
- A.2.** The causes can be as follows:
Etiologic classification:
- a. *Infective:*
 - i. Viral
 - ii. Pyogenic (Bacterial)
 - iii. Tuberculosis
 - iv. Mycotic
 - v. Parasitic.
 - b. *Non-infective:*
 - i. Acute myocardial infarction
 - ii. Uremia
 - iii. Neoplasms, i.e., primary or metastatic
 - iv. Myxoedema
 - v. Cholesterol
 - vi. Trauma
 - vii. Postradiation
 - viii. Idiopathic.
 - c. *Autoimmune disorders:*
 - i. Rheumatic fever
 - ii. Systemic lupus erythematosus
 - iii. Rheumatoid arthritis
 - iv. Scleroderma
 - v. Hydralazine and Procainamide
 - vi. Postmyocardial infarction (Dressler's syndrome)
 - vii. Postpericardiotomy syndrome.
- A.3.** This is an inflammation of the intercostal muscles produced by coxsackie B-5 virus and usually occurs in epidemics. This lasts for 7 to 10 days but can relapse.
- A.4.** This depends on the cause. However, it can lead to pericardial effusion and then tamponade. In case of tuberculous pericarditis, fibrosis occurs leading to constrictive pericarditis. Cardiac arrhythmias may also occur.

- A.5.** The treatment is according to the aetiology. However, mostly it is viral and requires no specific treatment. To get rid of the most disturbing symptom, i.e., pain, non-steroidal anti-inflammatory drugs are ideal if there is no contra-indication, e.g., indomethacin in a dose of 25 mg thrice a day after meals is quite effective. If it is tuberculous, then anti-tubercular therapy is indicated. Addition of corticosteroids may be helpful to prevent any adhesions between the layers of pericardium.

6

C A S E

Inferior Myocardial Infarction

BRIEF HISTORY

A man of 47 was admitted with a three-hour history of central chest pain and shortness of breath. His pain radiated to the left shoulder and lower jaw and was moderate-to-severe in intensity. He was diagnosed to have exertional angina three months ago and was advised to lose weight and take angised tablets as required. He had been tried 3 such tablets before coming to the hospital but with no relief. He had been attending a wedding party and ate heavy meals night before and thought the pain might have been due to indigestion, therefore, he had also tried some antacids, but this did not help the pain either. He had felt nauseated in the last two hours and had profuse, cold sweating on the forehead.

He had been fit and healthy until three months ago. He lived with his wife, had two sons, 18-and-16-years old. He had been smoking 25 cigarettes a day for over 25 years until three months ago when he stopped smoking on his doctor's advice. His father died at the age of 53, his mother was 68 and healthy and one brother, 51 was also in good health.

IMPORTANT CLUES ON CLINICAL EXAMINATION

On examination, he was obese, JVP was not raised. Blood pressure was 130/70 mmHg. Pulse was 68 per minute with occasional extrasystoles. Respiration was 20 per minute. There was no cyanosis, thyroid enlargement or lymphadenopathy. Heart sounds were normal. He had a soft, systolic, apical murmur with no radiation. Trachea was central. Breath sounds were normal with a few left basal crepitations. Examination of abdomen and central nervous system was normal.

INVESTIGATIONS

The following were the results of various investigations:

Hb:	14.9 g/dl	Bicarbonate:	23 mmol/l
	(normocytic normochromic)	Chloride:	103 mmol/l
WBC:	$9.7 \times 10^9/l$	Blood urea:	8.4 mmol/l (50 mg/l)
Platelets:	$300 \times 10^9/l$	Blood glucose:	8 mmol/l (144 mg/dl)
ESR:	39 mm in 1st hour	Urine:	normal
Sodium:	140 mmol/l	Chest X-ray:	heart size was normal
Potassium:	3.5 mmol/l	ECG:	as shown in Figure 6.1

DETERIORATION ON THE THIRD DAY OR FURTHER FOLLOW UP

His condition improved after treatment with morphine, oxygen and bed rest. However, on the third day, he suddenly became dyspnoeic and complained of tightness in his chest. His blood pressure dropped to 90/50 mmHg, pulse was 40 per minute and respiratory rate was 34 per minute. On examination at this stage, he was found to have developed a pansystolic apical murmur radiating to the left axilla. There was no evidence of deep vein thrombosis in the legs. His chest was full of crackles bilaterally. Examination of central nervous system and abdomen remained unremarkable.

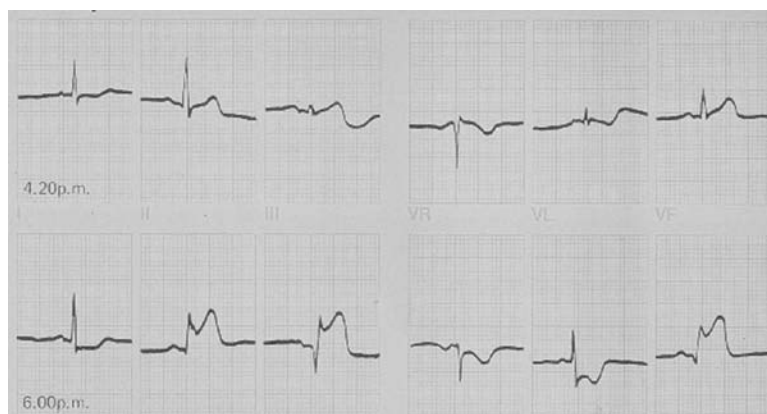


Fig. 6.1: Development of inferior infarction

QUESTIONS

- Q.1.** What is the most likely cause of this patients deterioration on the third day of his admission?
- Q.2.** How could you explain the pan-systolic murmur and what treatment could be offered?
- Q.3.** What happened on the third day?
- Q.4.** Name six complications of your diagnosed disease which may be seen within the first week.
- Q.5.** How would you clinically diagnose complete heart block?
- Q.6.** What is the role of streptokinase and tissue plasminogen activator (tPA)?

ANSWERS

- A.1.** Initial diagnosis in this forty-seven year old obese gentleman with history of smoking and family history of heart disease with recently diagnosed angina is ischaemic heart disease. But the onset of severe chest pain radiating to jaw and associated with sweating indicate an acute myocardial infarction. Papillary muscle rupture is not an uncommon complication in the first week and typically presents with signs of shock and left ventricular failure. The sudden appearance of pan systolic apical murmur, falling blood pressure, pulmonary congestion and tachypnoea are suggestive of this complication.
- A.2.** Papillary muscle rupture explains the pan-systolic murmur. It requires immediate assessment and treatment with:
- i. Morphine
 - ii. Oxygen
 - iii. Digoxin
 - iv. Inotropic support to increase the blood pressure adequately.
 - v. Consider surgical intervention in cases of failure of medical therapy. Intra-aortic balloon pump may be required till surgery is arranged.
- A.3.** The patient dropped his blood pressure and had bradycardia which indicated that he had developed complete heart block. He had also developed a new pan-systolic apical murmur suggestive of papillary muscle rupture.
- A.4.**
- i. Various cardiac arrhythmias
 - ii. Cardiogenic shock
 - iii. Congestive cardiac failure
 - iv. Pericarditis
 - v. Rupture of interventricular septum, chordae tendinae or the myocardium.
 - vi. Thrombo-embolism—systemic or pulmonary.
- A.5.** Clinically at the bed side, complete heart block can be recognised by:
- i. Marked bradycardia, i.e, less than 40 beats/minute
 - ii. Low blood pressure

- iii. Loud and variable 1st heart sound
 - iv. Cannon waves (giant “a” wave) in the jugular venous pressure.
- A.6.** Streptokinase, which is an enzyme derived from micro-organisms, if given in the first four hours of the onset of pain, produces very good results both clinically and electrocardiographically. Usual dose is 1.5 million units diluted in 100 c.c. of N. saline and infused over an hour. Tissue plasminogen activator (tPA) is better than streptokinase but is much more expensive. The dose is usually 10 mg IV start, then 50 mg over 1 hour then 40 mg over next two hours. Results are better than streptokinase.

7

CASE

Left Ventricular Aneurysm

BRIEF HISTORY

A 54-year-old man was admitted with a history of gradually increasing breathlessness for the last three months. A month prior to his recent visit, he developed sudden weakness of his left half of face and body which lasted for about 12 hours and gradually recovered. He also complained of swelling of both feet and had palpitations. There was history of dry cough but no sputum, haemoptysis or fever. On a few occasions, he had paroxysmal nocturnal dyspnoea. In the past four years, he has had two attacks of myocardial infarction and on the second occasion his stay was about two weeks in the hospital. He used to smoke 20 cigarettes a day but stopped smoking an year ago.

IMPORTANT CLUES ON CLINICAL EXAMINATION

On examination, he was breathless even at rest. Pulse was 110/min, regular. Blood pressure was 115/75 mmHg. His JVP was raised by 3 cm. Apex beat was diffuse and double in character. Heart sounds were feeble with an S3 gallop. Chest revealed bibasal crackles. There was pedal oedema. Liver was enlarged 3 cm below right subcostal margin and was tender and smooth in consistency. Neurological examination was unremarkable.

INVESTIGATIONS

Investigations revealed:

Hb:	14.5 g/dl	Chloride:	98 mmol/l
	(normocytic	Blood urea:	5.0 mmol/l (30 mg/l)
	normochromic)	Creatinine:	114 umol/l (1.3 mg/dl) l

Contd...

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WCC:	$8.9 \times 10^9/l$	Blood Sugar:	6 mol/l(108 mg/dl)
	P:72% L:18%	SGOT(AST):	60 U/l
	M:6%E:4%		
Platelets:	$280 \times 10^9/l$	SGPT(ALT):	45 U/l
ESR:	15 mm in	Bilirubin:	20 μ mol/l (1.2 mg/dl)
	1st hour		
Sodium:	139 mmol/l	Urine	
Potassium:	4.3 mmol/l	Examination:	2-4 pus cells/hpf
Bicarbonate:	26 mmol/l	ECG:	as shown in Figure 7.1

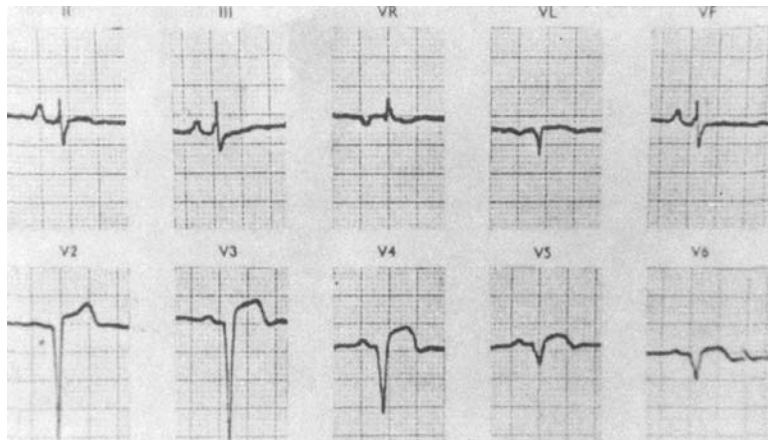


Fig. 7.1

QUESTIONS

- Q.1. What is the diagnosis?
- Q.2. Why did the patient develop hemiparesis?
- Q.3. What two further investigations can be done to confirm the diagnosis?
- Q.4. What treatment can be offered?

ANSWERS

- A.1.** In a patient who has had two heart attacks in the past and now is breathless even at rest with diffuse and double apex beat and typical ECG changes, a diagnosis of left ventricular aneurysm is indicated.
- A.2.** In left ventricular aneurysm, a part of the ventricle is akinetic or dyskinetic and often a thrombus is formed from where embolization can take place in the arterial system in any part of the body. If the thrombus remains there for a long time, then it can become calcified.
- A.3.** i. Echocardiogram which will show an akinetic or dyskinetic part of left ventricle and presence of a thrombus.
ii. Cardiac catheterization with radio-opaque dye where one can outline the aneurysm.
- A.4.** Medical treatment consists of diuretics and drugs which decrease the preload and afterload and surgical treatment consists of aneurysmectomy. If there is a risk of recurrent transient ischaemic attacks (TIA) or embolic strokes, then long-term anticoagulation with warfarin is mandatory.

Pulmonary Embolism

BRIEF HISTORY

A 45-year-old woman was admitted in gynaecology ward for hysterectomy because of recurrent vaginal bleeding due to fibroids. On the second postoperative day she spiked temperature of 100°F which lasted for one day only. She had a very low threshold for pain and was reluctant to mobilize. Otherwise she was progressing well. On the seventh postoperative day, she suddenly became breathless and started complaining of pain in the left side of chest. The pain was pleuritic in nature. There was no history of haemoptysis but dry cough was present.

IMPORTANT CLUES ON CLINICAL EXAMINATION

On examination, she was orthopnoeic, looked exhausted and there was central cyanosis as well. Pulse was 140 per minute regular and BP was 100/70 mmHg. Heart sounds revealed wide splitting of second heart sound. Chest expansion was diminished on the left side and there was decreased air entry. Abdominal and neurological examinations were normal. There was no evidence of deep venous thrombosis in the legs.

INVESTIGATIONS

Following investigations were performed:

Hb:	13.4 g/dl (normocytic normochromic)	Potassium:	3.4 mmol/l
		Bicarbonate:	26 mmol/l
		Chloride:	100 mmol/l
WCC:	$9.2 \times 10^9/l$	Blood urea:	5.0 mmol/l (30 mg/dl)
	P:78% L:18%	Blood sugar:	8 mmol/l (144 mg/dl)
	M:2%E:2%		

Contd...

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Platelets:	$350 \times 10^9/l$	Creatinine:	85 $\mu\text{mol/l}$ (0.9 mg/dl)
ESR:	10 mm in 1st hour	Urine:	normal
Sodium:	4.2 mmol/l		

QUESTIONS

- Q.1. What is the most likely diagnosis?
- Q.2. What three investigations are required urgently?
- Q.3. Name and discuss briefly two diagnostic investigations.
- Q.4. What treatment can be offered?

ANSWERS

A.1. In a woman who had undergone a major operation and on the seventh postoperative day becomes breathless with chest pain and clinically has tachycardia, tachypnoea and cyanosis favours a diagnosis of major pulmonary embolism.

A.2. These include:

- i. *ECG*: To rule out myocardial infarction and to confirm specific changes of pulmonary embolism, i.e., S wave in lead I, Q wave and inverted T wave in lead III. There is rightward shift of QRS complex and peaked P wave with ST-T changes indicating right ventricular strain.
- ii. *Chest X-ray*: It shows atelectasis, wedged shaped opacity with the base towards the periphery.
- iii. *Arterial blood gases*: They show hypoxia, hypocapnoea and respiratory alkalosis initially.

A.3. These are:

i. **Ventilation Perfusion Scan (V/Q scan)**

This is performed by intravenous injection of microspheres or macro aggregates of albumin (MAA) labelled with technetium-^{99m}Tc and radioactivity is measured. This shows perfusion of the lung parenchyma. A properly performed perfusion scan which is normal excludes the diagnosis of significant pulmonary embolism. On the other hand, a scan showing zones of absent radioactivity provides a substantial diagnostic support. Perfusion scan only, however, lack specificity in the presence of lung parenchymal diseases and, therefore, a ventilation scan with Xenon 133 or 127 is performed and mismatch between perfusion and ventilation is confirmatory of pulmonary embolism.

ii. **Pulmonary Angiography**

This provides anatomic information about the location of pulmonary embolus but is more invasive. Classically, the angiogram shows an abrupt "cut off" a vessel at the site of embolic lodgement. If it is concave distally, it shows a fresh embolus, but if it is convex distally, it shows an old embolus.

- A.4. i. Initially, intravenous heparin bolus of 15000 to 20000 units is given, then continuous intravenous infusion at approximately 1000 units per hour or 5000 to 7500 units are given intravenously after every four hours. Repeated APTT should be performed.
- ii. Thrombolytic therapy, such as streptokinase and urokinase, can hasten the resolution of emboli.
- iii. Surgical therapy should be reserved for those patient in whom heparin therapy is inadequate or impracticable. In such cases, pulmonary embolectomy must be considered.

9

C A S E

Empyema

BRIEF HISTORY

A 43-year-old man was admitted to medical ward via accident emergency department with a four-day-history of fever with rigors and sweats at night. He also complained of discomfort in the right side of chest and it used to get worse on coughing and sneezing. He had decreased appetite and also had lost about 4 kg in weight during this course of illness. Two weeks prior to the present illness, he had high grade fever and pleuritic pain on the same side and was admitted to a hospital where, according to the patient, some fluid was taken out from his right side of the chest, but then he improved with antibiotics. He had no family history of chest or heart disease and there was no history of hypertension or diabetes. He smoked 15 to 20 cigarettes a day. No allergies were noticed.

IMPORTANT CLUES ON CLINICAL EXAMINATION

On examination, he looked toxic and obviously in discomfort. Temperature was 103°F and there was no pallor, cyanosis, jaundice, clubbing or lymphadenopathy. BP was 145/92 mmHg and pulse was 118 per minute. Chest examination revealed decreased expansion on the right side of the chest, stony dull on percussion with decreased air entry on auscultation in the right lower chest. Cardiovascular, abdominal and neurological examinations were normal.

INVESTIGATIONS

Following investigations were carried out:

Hb:	12.8 g/dl (normocytic normochromic)	Bicarbonate:	24 mmol/l
		Chloride:	99 mmol/l
WCC:	14.8x10 ⁹ /l P:76% L:20% M:2%E:2%	Blood urea:	9 mmol/l (54 mg/dl)
		Blood sugar:	6 mmol/l (108 mg/dl)
		Creatinine:	138 umol/l (1.5 mg/dl)
Platelets:	300 × 10 ⁹ /l	Urine:	normal
ESR:	74 mm in 1st hour	ECG:	sinus tachyardia, no evidence of ischaemia
Sodium:	138 mmol/l		
Potassium :	4.2 mmol/l		

QUESTIONS

- Q.1.** What is the most likely diagnosis?
- Q.2.** What may be the aetiology?
- Q.3.** What further investigations would you ask for?
- Q.4.** What treatment can be offered?

ANSWERS

- A.1.** There is a history of chest infection two weeks prior to admission and some fluid was taken out from his chest. That was most probably a pneumonia with effusion but later on with a history of persistent fever, chest pain and clinical evidence of pleural fluid with leukocytosis indicates that this patient has now developed empyema on the right side of the chest, a complication of thoracentesis or unresolved postpneumonic pleural effusion.
- A.2.** In majority of cases it is the spread from contiguous structures, i.e., lung abscess, oesophageal perforation, subdiaphragmatic abscess, haematogenous spread (more common in children), thoracic surgery or instrumentation of the pleural space (thoracentesis) as happened in the case above.
- A.3.** These include:
- i. *Chest X-ray* to show pleural effusion and status of underlying lung.
 - ii. *Ultrasound of chest* for exact localization and see if there are loculations.
 - iii. *Thoracentesis*: It may reveal thick, purulent liquid with high leukocyte count, high proteins and low glucose concentration. Gram stain will show the causative organisms which might be *Staphylococci*, *Pseudomonas*, *Klebsiella*, *E. coli*, *Pneumococci* and anaerobes.
 - iv. Z-N staining for acid-fast bacilli.
- A.4.** Most important step is to drain the fluid through chest intubation in addition to antimicrobial therapy.
- If the fluid is thin, then drainage may be achieved by repeated thoracentesis.
- If the fluid is loculated, then multiple thoracostomy tubes may be needed. In addition to this, fibrinolytic agents may be tried.
- If there is persistent fever and no general improvement within a week, then limited thoractomy is indicated in which small portion of overlying rib is resected and pleural adhesions are broken down manually.
- If this also fails, then decortication (pleural peel) is performed.
- Patients with underlying serious diseases, old age and in whom the treatment is delayed carry increased mortality.

10

C A S E

Pulmonary Tuberculosis

BRIEF HISTORY

A 52-year-old man attended the outpatient department with a history of low-grade fever, cough, purulent sputum for the last three months. He told that his chest had never been right as he had recurrent chest infections and for the last three months, he had noticed some blood in his sputum. Six months ago, he was diagnosed to suffer from diabetes mellitus for which he was taking some medications. He complained of easy fatigueability and weight loss with night sweats. He had been a heavy smoker. No allergies were noticed.

IMPORTANT CLUES ON CLINICAL EXAMINATION

On examination, he was rather anxious. Temperature was normal. There was mild cyanosis of the tongue but no lymphadenopathy, clubbing or jaundice was seen. Pulse was 88 per minute, regular and BP was 140/85 mmHg. Chest revealed fine rhonchi bilaterally, but coarse crackles over the right upper and mid zone. Abdominal, cardiovascular and neurological examinations were normal.

INVESTIGATIONS

Investigations included:

Hb:	12.2 g/dl (normocytic normochromic)	Blood urea:	11.3 mmol/l(68 mg/dl)
		Creatinine:	90 umol/l (1.0 mg/dl)
WCC:	$9.9 \times 10^9/l$ P:64% L:33% M:2%E:1%	Blood sugar:	14 mol/l (252 mg/dl)
		Urine:	traces of proteins, sugar++
		ECG:	normal

Contd...

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Platelets:	$240 \times 10^9/l$	Chest X-ray:	hyper-inflated chest,
ESR:	98 mm in 1st hour		infiltrations
Sodium:	139 mmol/l		in the right upper
Potassium:	4.5 mmol/l		and middle zones
Bicarbonate:	25 mmol/l		
Chloride:	101 mmol/l		

QUESTIONS

- Q.1. What is the diagnosis?
- Q.2. What other serious condition should be ruled out?
- Q.3. What further four investigations would you ask for?
- Q.4. What treatment can be offered?
- Q.5. Describe side effects of the drugs used for treatment.

ANSWERS

- A.1.** A patient, who has been a heavy smoker and had chronic bronchitis, developed diabetes mellitus and then haemoptysis with classical, clinical and radiological features suggest pulmonary tuberculosis.
- A.2.** Bronchogenic carcinoma can present in the same way and it is important in the differential diagnosis.
- A.3.**
- Sputum for AAFB and malignant cells.
 - Mantoux test (it has limited diagnostic value in endemic areas).
 - Computerized tomography of the lung.
 - Bronchoscopy, and/or bronchial washings or biopsy, if a lesion is present.
- A.4.** Mostly, it is the medical treatment in pulmonary tuberculosis. The dose of drugs used depend on the weight of the patient.
- A.** *If less than 50 kg*
- Isoniazid 300 mg daily
 - Rifampicin 450 mg daily
 - Ethambutol 900 mg daily
 - Pyrazinamide 1500 mg daily
- All used for further two months, then (i), (ii) and (iii) are used for six more months to complete the course.
- B.** *If more than 50 kg*
- Isoniazid 300 mg daily
 - Rifampicin 600 mg daily
 - Ethambutol 1200 mg daily
 - Pyrazinamide 2000 mg daily
- This is for two months, then (i), (ii) and (iii) for further six months. Tab. Pyridoxine 50 mg daily is supplemented with it to prevent peripheral neuropathy.
- A.5.**
- Isoniazid—peripheral neuropathy, hepatitis
 - Rifampicin—enzyme inducer, hepatotoxicity
 - Ethambutol—optic neuritis and colour vision disturbances.
 - Pyrazinamide—hepatotoxicity.

11

C A S E

Atypical Pneumonia

BRIEF HISTORY

A 26-year-old man was admitted with a six-days-history of flu-like symptoms, malaise, headaches, chest pain and unproductive cough. He complained of fever with rigors and felt extremely weak. He did mention a little trouble in his left ear. For the last three-days he was taking ampicillin without any benefit. In the past he had always been fit and healthy. There were no other significant systemic symptoms.

He was a smoker and smoked twenty cigarettes per day. No allergies were noticed.

IMPORTANT CLUES ON CLINICAL EXAMINATION

On examination, he looked toxic, disorientated and dehydrated. Blood pressure was 150/85 mmHg. Pulse was 96 per minute and regular. Temperature was revealed 101.4°F. Thyroid and lymph nodes were not enlarged. No clubbing or oedema was noticed. Trachea was central and breath sound revealed widespread crepitation without pleural rub or bronchial breathing. Left auroscopy showed bulging tympanic membrane. Abdominal, cardiovascular and neurological examinations were normal.

INVESTIGATIONS

Following were the investigations:

Hb:	13.9 g/dl	Bicarbonate: 23 mmol/l
	(normocytic	Chloride: 98 mmol/l
	normochromic)	Blood urea: 10.8 mmol/l (65 mg/dl)

Contd...

Contd...

WCC:	13.9 × 10 ⁹ /l	Creatinine:	140 umol/l (1.6 mg/dl)
	P:92% L:6%	Blood sugar:	8.5 mmol/l(153 mg/dl)
	M:1%E:1%		
Platelets:	250 × 10 ⁹ /l	Urine:	normal
ESR:	69 mm in 1st hour	ECG:	normal sinus rhythm
Sodium:	139 mmol/l		with ventricular ectopics
Potassium:	4.1 mmol/l		

QUESTIONS

- Q.1.** What is his most likely diagnosis?
- Q.2.** What four investigations will you ask for?
- Q.3.** Name two antibiotics which are helpful in the treatment.
- Q.4.** What are the complications of this illness?

ANSWERS

- A.1.** The most likely diagnosis in this young patient with clinical features of pneumonia with no response to ampicillin, is some form of atypical pneumonia, most probably mycoplasma pneumonia. Bulging tympanic membrane (bullous myringitis) further helps the diagnosis.
- A.2.**
- i. Chest X-ray.
 - ii. Sputum for culture and sensitivity if possible.
 - iii. Blood cultures.
 - iv. Serology—to look for rising titres of specific antibodies—at the day of admission and on the 10th day.
- A.3.**
- i. Tetracyclines.
 - ii. Erythromycin, clarithromycin.
- A.4.** These include:
- i. Meningoencephalitis
 - ii. Polyneuritis
 - iii. Bullous myringitis
 - iv. Stevens-Johnson syndrome
 - v. Myocarditis
 - vi. Haemolytic anaemia—cryoglobulinaemia.

12

C A S E

Pleural Effusion

BRIEF HISTORY

A 62-year-old woman attended outpatient department with two-month history of progressive shortness of breath on exertion, undue tiredness, poor appetite and loss of weight. There was no history of cough, expectoration or haemoptysis. There were no urinary or bowel symptoms and she was not taking any drugs. She did mention that she felt a little sweaty and feverish at night. Her husband had some respiratory problems for which he was treated with medicines for many months.

IMPORTANT CLUES ON CLINICAL EXAMINATION

On examination, she was dyspnoeic. JVP was not raised. There was no anaemia, clubbing, cyanosis, oedema or lymphadenopathy. Trachea was central. Over her right base posteriorly, she had dullness on percussion with absent breath sounds. Apex beat was in left fourth intercostal space well inside midclavicular line. She had no heart murmurs. Examinations of abdomen and central nervous system were normal.

INVESTIGATIONS

Following were the results of various investigations:

Hb:	11.6g/dl (normocytic normochromic)	Bicarbonate:	24 mmol/l
		Chloride:	98 mmol/l
		Blood sugar:	13.3 mmol/l (23.9 mg/dl)
WCC:	$8 \times 10^9/l$	Blood urea:	7.5 mmol/l (45 mmg/dl)
	P:72% L:25%	Creatinine:	87 umol/l (0.9 mg/dl)
	M:2% E:1%	Urine analysis:	protein ++

Contd...

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Platelets:	$320 \times 10^9/l$	ECG:	normal
ESR:	68 mm in 1st hour	Chest X-ray:	as shown in the Figure 12.1
Sodium:	137 mmol/l		
Potassium:	3.3 mmol/l		



Fig. 12.1

QUESTIONS

- Q.1.** What is the most likely diagnosis?
- Q.2.** What is the differential diagnosis?
- Q.3.** What three investigations will you ask for?
- Q.4.** Name three conditions causing such X-ray appearance.

ANSWERS

- A.1.** It is obvious from the physical examination and investigations that she has right pleural effusion and diabetes mellitus (high blood glucose). Tuberculosis often has atypical presentation in the elderly and the absence of a cough or expectoration should not be, therefore, surprising. Diabetic patients are prone to conditions, such as tuberculosis, hence, tubercular pleural effusion is most likely to be the case in this lady which is further strengthened by the fact that her husband may have had pulmonary tuberculosis, too.
- A.2.**
- i. Malignancy—Malignant pleural effusion.
 - ii. Pneumonia—Post-pneumonic pleural effusion.
 - iii. Connective tissue diseases. A part of polyserositis. The effusion is exudative.
- A.3.**
- i. Ultrasound of the chest and aspiration of pleural fluid for cytology, AFB and biochemistry.
 - ii. Pleural biopsy.
 - iii. Bronchoscopy.
- A.4.**
- i. Congestive heart failure.
 - ii. Nephrotic syndrome.
 - iii. Cirrhosis of liver. The effusion is transudative.

13

C A S E

Lobar Pneumonia

BRIEF HISTORY

A 34-year-old man was brought to accident and emergency department with four-day history of high grade fever and rigors. The illness started with generalized aches and pains and then he developed cough which was dry to begin with but later on became productive. He also complained of severe chest pain on the right side, especially on deep breathing and coughing. He had enjoyed good health, but smoked 10 to 15 cigarettes a day.

He was treated by local doctors with injections and tablets but there was little relief of his symptoms. He coughed rusty coloured sputum in the casualty department.

IMPORTANT CLUES ON CLINICAL EXAMINATION

On examination, he was confused with toxic look and had a temperature of 104°F. His pulse was 130 per minute and BP was 120/70 mm Hg. He looked pale but was not cyanosed or jaundiced and there was no lymphadenopathy either. His breathing was very rapid and there were few crusty, papular lesions over his upper lip too. Chest examination revealed dullness to percussion on the right side with bronchial breathing. Cardiovascular, abdominal and neurological systems were normal.

Investigations were carried out as follows:

Hb:	12.5 g/dl (normocytic normochromic)	Bicarbonate:	22 mmol/l
		Chloride:	96 mmol/l
		Blood urea:	6 mmol/l (36 mg/dl)
WBC:	29×10 ⁹ /l	Creatinine:	70 umol/l (0.8 mg/dl)
	P:86% L:8% M:2%	Blood sugar:	7.2 mmol/l (129 mg/dl)

Contd...

Contd...

Bandcells:	4%	Urine:	normal
ESR:	30 mm in 1st hour	ECG:	sinus tachycardia
Sodium:	135 mmol/l		without ischaemia
Potassium:	4.5 mmol/l		

QUESTIONS

- Q.1. What is the most likely diagnosis?
- Q.2. What other investigations would you ask for?
- Q.3. Which side you think is the trachea shifted?
- Q.4. What are the pathological stages of this diagnosis?
- Q.5. List a few complications of this disease.

ANSWERS

- A.1.** In a young male, sudden onset of high fever with pleuritic chest pain and coughing up rusty sputum with clinical evidence of consolidation in the right side of the chest indicates right lower lobar pneumonia.
- A.2.**
- i. Sputum examination for Gram staining and AAFB.
 - ii. Arterial blood gases.
 - iii. Blood cultures.
 - iv. X-ray chest PA view.
- A.3.** The trachea remains central as there is consolidation and the lung parenchyma is neither pushed or pulled in any direction.
- A.4.**
- i. Inflammatory cell infiltration.
 - ii. Grey hepatization.
 - iii. Red hepatization.
 - iv. Resolution.
- A.5.** These can be divided into local and distant complications:
- Local complications include:*
- i. Atelectasis of whole or part of the lung.
 - ii. Delayed resolution.
 - iii. Abscess formation.
 - iv. Pleural effusion.
 - v. Empyema.
 - vi. Pericarditis.
- Distant complications include:*
- i. Septic arthritis.
 - ii. Metastatic abscesses.
 - iii. Septicaemia.
 - iv. Paralytic ileus.
 - v. Liver dysfunction.

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C A S E

Bronchiectasis

BRIEF HISTORY

A 28-year-old man attended the outpatient clinic with a long history of cough and copious amount of purulent sputum. He could recall this since his childhood. The cough and sputum had decreased in severity on quite a few occasions. A week prior to his visit, he had coughed some bright red blood mixed with sputum. He also complained of increased breathlessness after a bout of cough or exertion. There was no history of fever, but he did complain of malaise, lethargy and weakness. In the past, he had whooping cough, but there was no history of diarrhoea or vomiting. He was a non-smoker.

IMPORTANT CLUES ON CLINICAL EXAMINATION

On examination, he looked emaciated. Temperature was 98.4°F. He had clubbing of his fingers. Pulse was 86 per minute and regular. BP was 125/80 mmHg. Chest examination revealed coarse crackles on both bases. No pleural rub was audible. Cardiovascular, abdominal and neurological examinations were normal.

INVESTIGATIONS

Investigations included:

Hb:	10.8 g/dl (normocytic normochromic)	Bicarbonate:	23 mmol/l
		Sputum:	numerous pus cells and bacteria
WBC:	11.4×10^9 /l P:78% L:20% M:2%	Chest X-ray:	prominent broncho vesicular marking in both lower

Contd...

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ESR:	56 mm in 1st hour	zones, cardiac size normal
Sodium:	136 mmol/l	
Potassium:	3.8 mmol/l	

QUESTIONS

- Q.1.** What is the diagnosis?
- Q.2.** What further investigations are required to confirm the diagnosis?
- Q.3.** Name a few complications of this disease.
- Q.4.** What is the treatment?
- Q.5.** What are associated clinical syndromes with this disease?

ANSWERS

A.1. In a patient with long standing history of cough and large amounts of sputum with clubbing and a past history of whooping cough suggest the diagnosis of bronchiectasis.

A.2. *CT scan of the chest:*

Bronchography: This may show cystic areas if the peripheral airways are affected. The lower lobes are most commonly affected, the left being more commonly than right. This is indicated only if surgery is to be undertaken.

Immunological status of the patient:

Microbiology: The most common infecting organism is *Haemophilus influenzae* but anaerobic infections also occur.

- A.3.**
- i. Chronic sinusitis is a frequent complication
 - ii. Recurrent pneumonia
 - iii. Pleurisy
 - iv. Brain abscess
 - v. Haemoptysis which may be life-threatening
 - vi. Amyloidosis.

A.4. This can be either medical or surgical:

- i. *Medical treatment:* It consists of combination of chest physiotherapy and antibiotics. Postural drainage is very important. Oxytetracycline, cotrimoxazole, ampicillin or amoxycillin are first line antibiotics. Doxycycline (vibramycin) can also be used. Quinolone derivatives like ofloxacin. (Tarivid), such as and ciprofloxacin (ciproxin), can also be used if there is a mixed type of infection.
- ii. *Surgical treatment:* It is not offered so often as it used to be 20 to 30 years ago as antibiotics are quite effective now. However, if the disease is localised with recurrent chest symptoms, then it is the treatment of choice. Main contraindications to surgery are diffuse disease and generalised airway obstruction.

- A.5. i. *Kartagener's syndrome*: It consists of situs inversus, paranasal sinusitis and bronchiectasis. It is autosomal recessive and main pathophysiological defect is in the ciliary ultrastructure. In Young's syndrome there is ciliary dysfunction and no defect in the ultrastructure. Other findings are the same as in Kartagener's syndrome.
- ii. *The yellow nail syndrome*: It consists of yellow nails, lymphoedema, pleural effusion and bronchiectasis.
- iii. *Riley-Day syndrome*: It is also called familial dysautonomia and is transmitted as autosomal recessive trait and is found exclusively in Jewish infants of Ashkenazi origin. Basic defect is in the autonomic nervous system.
- iv. *Cystic fibrosis*: It is autosomal recessive and results from disordered exocrine function with viscid secretions.

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C A S E

Lung Abscess

BRIEF HISTORY

A 55-year-old man presented to accident and emergency department with a history of haemoptysis. The blood he coughed was fresh, bright red with a few clots in it. He gave history of pneumonia about two months ago which, according to him, got complicated and he was given a number of antibiotics while in the hospital. He complained of undue tiredness, malaise and fever with rigors and sweating. He did mention that since his discharge from the hospital, he had been coughing up greenish sputum which sometimes was copious in amount but never coughed blood like this before. He smoked 15 to 20 cigarettes a day. He was not known hypertensive or diabetic and there was no history of tuberculosis either.

IMPORTANT CLUES ON CLINICAL EXAMINATION

On examination, he looked toxic and anxious. Temperature was 100°F. General physical examination revealed pallor and clubbing of fingers. Pulse was 100 per minute and regular. JVP was not raised and heart sounds were normal. Chest showed central trachea with bronchial breathing in the right midzone. Course crackles were also present there. Abdominal and neurological examinations were unremarkable.

INVESTIGATIONS

Investigations included:

Hb :	11.4 g/dl (normocytic normochromic)	Blood sugar	6 mmol/l (115 mg/dl)
		Urine:	normal
		Sputum:	

Contd...

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WCC:	19.7 × 10 ⁹ /l P:80% L:15% M:3% E:2%	examination:	gram+ve cocci numerous pus cells
ESR:	75 mm in 1st hour	ECG:	normal sinus rhythm
Blood urea:	6.0 mmol/l (34 mg/l)	Chest X-ray:	as shown in Figure 15.1
Creatinine:	126 µmol/l (1.0 mg/dl)		

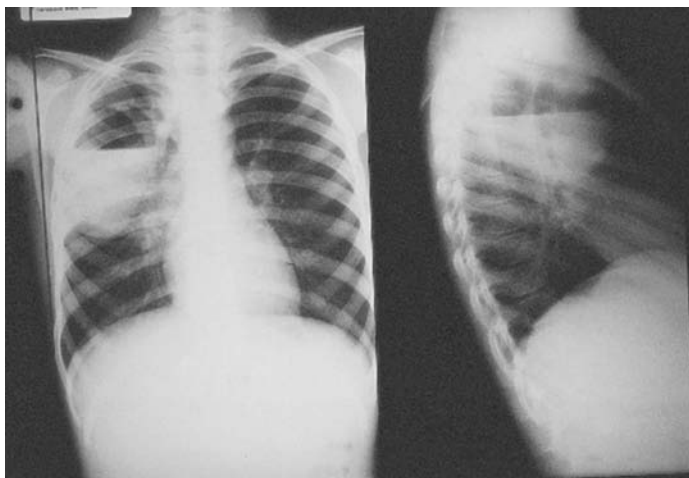


Fig. 15.1

QUESTIONS

- Q.1. What is the diagnosis?
- Q.2. What is the differential diagnosis?
- Q.3. What are the complications of this disease?
- Q.4. What is the treatment?

ANSWERS

- A.1.** The patient is a smoker, had pneumonia and now coughed up blood with history of fever and X-ray findings all suggest a lung abscess.
- A.2.** Same picture can be seen in bronchogenic carcinoma. When there is malignancy, it can cavitate and superadded infection and necrosis would present in the same way. Other conditions to rule out include pulmonary tuberculosis, actinomycosis or cavitating pulmonary infarct. Multiple cavitating opacities are seen with tuberculosis, pulmonary metastases and Wegeners granulomatosis.
- A.3.** These can be divided into:
- A. Local complications:**
 - i. Severe haemoptysis
 - ii. Multiple lung abscesses (satellite abscess)
 - iii. Empyema
 - iv. Suppuration to local vital structures.
 - B. Remote complications:**
 - i. Metastatic abscesses, e.g. brain, kidney.
 - ii. Amyloidosis.
- A.4.**
- i. **Antibiotics:** Specific infections such as *Staphylococci* or *Klebsiella*, will be treated with appropriate antibiotics. Benzyl penicillin is quite effective in the more common lung abscess in high doses. If anaerobic bacteria are present, addition of metronidazole is valuable.
 - ii. **Bronchoscopy:** It is advisable both to exclude a tumour and to aspirate secretions. Fibreoptic bronchoscopy is preferred for upper lobe abscesses, while rigid ones are good for aspiration of large volume of pus.
 - iii. **Postural drainage:** It may aid resolution of an abscess.
 - iv. **Surgical excision:** It is rarely required.

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C A S E

Bronchogenic Carcinoma

BRIEF HISTORY

A 61-year-old man was admitted with history of progressive cough, mucoid sputum and haemoptysis for the last three weeks. He had smoked 20 cigarettes a day for over forty years and had a smoker's cough in the morning for over 13 years. Before this, he had been treated for chest infection with antibiotics, but it did not get better. He had good appetite and had not lost weight recently. There was no history of chest pain, palpitations, urinary or bowel problems.

IMPORTANT CLUES ON CLINICAL EXAMINATION

On examination, he looked well. JVP was not raised. There was no anaemia or cyanosis. Lymph nodes and thyroid were not enlarged. He had early clubbing of his fingers, more marked on the left side. Trachea was central. He had an area of bronchial breathing with a few crepitations at his right base. Examinations of cardiovascular, abdomen and nervous system were unremarkable. A day after his admission, he had a grand mal epileptic fit.

INVESTIGATIONS

Investigations were as follows:

Hb:	11.4 g/dl (normocytic normochromic)	Bicarbonate: 25 mmol/l Chloride: 101 mmol/l
WCC:	$9.7 \times 10^9/l$ P:78% L:19% M:2% E:1%	Blood urea: 5.0 mmol/l (30 mg/dl) Creatinine: 128 μ mol/l (1.4 mg/dl) Blood Sugar: 6 mmol/l(108 mg/dl)

Contd...

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Platelets:	$300 \times 10^9/l$	Urine:	normal
ESR:	39 mm in 1st hour	ECG:	normal sinus rhythm, no ischaemic changes
Sodium:	136 mmol/l		
Potassium:	4.1 mmol/l		

QUESTIONS

- Q.1.** What is the most likely diagnosis?
- Q.2.** Give four investigations to help the diagnosis?
- Q.3.** Give four 'endocrinopathies' which may be associated with this disease.
- Q.4.** Give two major contraindications for surgical resection in patients with this disease.

ANSWERS

- A.1.** The most likely diagnosis in this man who has been a moderately heavy smoker with cough, haemoptysis, clubbing, bronchial breathing and epileptic fit is carcinoma of bronchus with possible collapsed lung and a patent bronchus and brain metastases.
- A.2.**
- i. Chest X-ray
 - ii. Sputum cytology for malignant cells, culture sensitivity and AAFB
 - iii. Bronchoscopy and biopsy.
 - iv. CT scan of the brain.
- A.3.**
- i. Hypercalcaemia due to ectopic parathyroid hormone secretion.
 - ii. Inappropriate ADH secretion.
 - iii. Inappropriate ACTH secretion.
 - iv. Carcinoid syndrome.
- A.4**
- i. Inadequate ventilatory function (FEV1 below 60 percent of predicted value).
 - ii. Evidence of metastases, e.g. in pleura, liver, brain, bone, etc.

BRIEF HISTORY

A 54-year-old man was admitted with fourteen-month history of progressive shortness of breath on exertion. There was no history of wheezing or diurnal variation. For last one month, he had started having an unproductive cough, and two weeks ago, he had arthralgia involving his ankle and knee joints which settled with paracetamol tablet within three days. There was no history of chest pain, loss of weight or appetite.

He had no pets at home. He had ulcerative colitis for the last twelve years, but for the last three years, his colitis was quiet and he was not taking any drugs.

IMPORTANT CLUES ON CLINICAL EXAMINATION

On examination, he was dyspnoeic and centrally cyanosed. There was marked clubbing of his fingers but had no enlargement of lymph nodes or thyroid. Blood pressure was 160/90 mmHg, and pulse was 88 per minute and regular. There was pitting oedema of both his ankles and the JVP was raised by 8 cm. Skin was normal with no subcutaneous nodules or ulceration. Trachea was central, but the chest expansion was limited, and he had bilateral fine inspiratory crepitations over his lung bases. He was in sinus rhythm but had left parasternal heave and a loud pulmonary component of second heart sound. His liver was 3 cm enlarged, soft and tender with no associated splenomegaly or ascites. Examination of the nervous system was normal.

INVESTIGATIONS

Following results of investigations were available:

Hb:	13.9g/dl (normocytic normochromic)	Blood glucose:	6.7 mmol/l (120 mg/dl)
		Blood urea:	4.6 mmol/l (27.6 mg/dl)
		Creatinine:	85 μ mol/l (0.9 mg/dl)
WCC:	8×10^9 /l P:82% L:16% M:2%E:1%	Serum bilirubin:	16 μ mol/l (0.9 mg/dl)
		Albumin:	3.3 g/dl
		Peak flow:	200 l/min
Platelets:	310×10^9 /l	Urine analysis:	normal
ESR:	42 mm in 1st hour	ECG:	prominent P waves, right axis deviation and right ventricular hypertrophy
Sodium:	139 mmol/l		
Potassium:	3.4 mmol/l		
Bicarbonate:	27 mmol/l		
Chloride:	100 mmol/l		

QUESTIONS

- Q.1.** What is the most likely diagnosis?
- Q.2.** What further six investigations will help diagnosis?
- Q.3.** Name four diseases known to be associated with your primary diagnosis.
- Q.4.** What is the cause of hepatomegaly and oedema?

ANSWERS

- A.1.** The most likely diagnosis in this man with progressive dyspnoea, no wheezing or diurnal variation, unproductive cough, central cyanosis, clubbing and bilateral fine basal crackles on inspiration is idiopathic or cryptogenic fibrosing alveolitis. Further, left parasternal heave with loud P₂, raised JVP, ankle oedema and hepatomegaly suggest that this patient has developed cor Pulmonale.
- A.2.**
- i. Chest X-ray (showing honeycombing of the lung parenchyma).
 - ii. Lung function test—restrictive lung functions and reduced CO diffusing capacity.
 - iii. Antinuclear antibodies (associated with autoimmune disorders).
 - iv. Blood gases (low PO₂, high PCO₂).
 - v. CT scan of chest showing classical appearance of the lungs.
 - vi. Lung biopsy (infiltration of chronic inflammatory cells and fibroblastic reaction).
- A.3.**
- i. Systemic lupus erythematosus
 - ii. Rheumatoid arthritis.
 - iii. Dermatomyositis/polymyositis.
 - iv. Systemic sclerosis.
- A.4.** Fibrosing alveolitis causes pulmonary hypertension and leads to failure of the right heart thus causing hepatomegaly and oedema.

*Cholangitis***BRIEF HISTORY**

A 62-year-old woman was admitted with two-day-history of severe right-sided abdominal pain and vomiting. She also felt febrile and had shakes with it. There was no history of cough, expectoration or chest pain. The pain was constant in the right hypochondrium without any radiation. She had not been able to eat or drink much because of this illness.

IMPORTANT CLUES ON CLINICAL EXAMINATION

On examination, her temperature was 101°F. Blood pressure was 90/50 mmHg. Pulse was 120 per minute and regular. JVP was not raised. There was no anaemia, clubbing, thyroid or lymph node enlargement. She was quite dehydrated and mildly icteric. On abdominal examination, there was marked guarding and tenderness in her right hypochondrium, but there was not definite hepatomegaly. Spleen was not palpable and there was not ascites either. Bowel sounds were audible. Respiratory, cardiovascular and neurological examinations were normal.

INVESTIGATIONS

Following were the results of various investigations:

Hb:	14.8 g/dl (normocytic normochromic)	Creatinine:	138 umol/l (1.5 mg/dl)
		Bilirubin:	28 umol/l (1.6 mg/dl)
WCC:	24 × 10 ⁹ /l	Total proteins:	5.8 g/dl
	P:88% L:8%	Albumin:	2.8 g/dl
	M:2% E:2%	Blood Culture:	E coli growth sensitive to cephalosporin.

Contd...

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Platelets:	310 × 10 ⁹ /l		
ESR:	73 mm in 1st hour	Urine:	out put in twenty four hours was 90 ml only.
Sodium:	132 mmol/l	ECG:	sinus rhythm, no evi- dence of acute ischaemia
Potassium:	3.9 mmol/l		
Bicarbonate:	24 mmol/l		
Chloride:	100 mmol/l	Chest X-ray:	normal
Blood sugar:	7.7 mmol/l (138 mg/dl)		
Blood urea:	8 mmol/l (48 mg/dl)		

QUESTIONS

- Q.1.** What is the most likely diagnosis?
- Q.2.** Give four common organisms responsible for such a serious condition.
- Q.3.** Give three common sources of these organisms.
- Q.4.** Give four antibiotics which may be used to treat this condition.
- Q.5.** What is the long-term prognosis of this condition?
- Q.6.** What is the diagnostic test for this patient after stabilization?

ANSWERS

- A.1.** The most likely diagnosis in this lady with high grade fever and rigors, right hypochondric pain, vomiting, low blood pressure, oliguria, raised white cell count and positive blood culture is septicaemia, probably, caused by biliary tract disease with ascending cholangitis.
- A.2.** i. *E. coli*
ii. *Klebsiella*
iii. *Pseudomonas aeruginosa*
iv. *B. proteus*.
- A.3.** i. Urinary tract infection with or without catheterisation.
ii. Respiratory tract infections.
iii. Skin sores especially in elderly patients.
- A.4.** i. Gentamycin
ii. Cephalosporins—third generation.
iii. Carbenicillin
iv. Kanamycin.
- A.5.** If not treated properly, this can develop into sclerosing cholangitis which is rare, chronic, inflammatory lesion and results in focal or diffuse fibrosis of the biliary ducts. Basically, it is divided into primary which is also called idiopathic and secondary which may be due to stones, cancer, trauma or contiguous infection. It presents with right upper quadrant pain, intermittent jaundice, pruritus and cholangitis. It may complicate into secondary biliary cirrhosis, portal hypertension, bleeding oesophageal varices and acute hepatic failure.
- A.6.** Endoscopic retrograde cholangio-pancreatography (ERCP).

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C A S E

Oesophageal Varices

BRIEF HISTORY

A 65-year-old man was brought to the accident and emergency department with a history of vomiting of copious amount of blood. The relatives did mention that he also vomited blood one day prior to this and passed dark-coloured stools. He also felt dizzy at that time. He was not a known hypertensive or diabetic but smoked ten cigarettes a day. Three years ago, he had an attack of jaundice which lasted for two weeks. The wife told that he complained of generalised weakness and bloating of his abdomen for the last three weeks.

IMPORTANT CLUES ON CLINICAL EXAMINATION

On examination, he was drowsy and sweating profusely. Restlessness was also evident. He looked cachectic and pale. Pulse was 120 per minute and regular but low volume. BP was recorded as 80 mmHg systolic only. Heart sounds were normal. Chest was clear. Abdomen showed tense ascites. Liver was not palpable. Neurological examination showed bilateral upgoing plantars.

INVESTIGATIONS

Investigations included:

Hb:	5.5 g/dl (normocytic normochromic)	Blood sugar: 4 mol/l(72 mg/dl) Blood urea: 14 mmol/l (84 mg/dl) Creatinine: 110 umol/l (1.2 mg/dl)
WCC:	$10.6 \times 10^9/l$ P:72% L:22% M:4% E:2%	Urine: protein++, blood++ ECG: sinus tachycardia, no evidence of ischaemia

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Platelets:	140 × 10 ⁹ /l	Chest X-ray: clear lung fields,
ESR:	64 mm in 1st hour	normal cardiac size
Sodium:	138 mmol/l	
Potassium:	5.2mmol/l	
Bicarbonate:	24 mmol/l	
Chloride:	99 mmol/l	

QUESTIONS

- Q.1. What is the immediate diagnosis?
- Q.2. What is the underlying pathology?
- Q.3. How would you manage such a patient?

ANSWERS

- A.1.** A patient with a history of jaundice in the past and now tense ascites who suddenly had a bout of haematemesis leading to shock suggest bleeding oesophageal varices.
- A.2.** The underlying diagnosis is cirrhosis of the liver which progressed to portal hypertension. Spleen is difficult to palpate in tense ascites.
- A.3.** This requires coordinated medical and surgical efforts.
- i. *Replacement of the blood lost:* It is advisable to use fresh blood.
 - ii. *Endoscopy:* Urgent endoscopy should be performed once the patient is revived from shock and the bleeding points may be seen other than bleeding oesophageal varices, and if there are varices, then sclerotherapy with absolute alcohol or STD (sodium tetradecyl sulphate) can be performed. Sometimes, the bleeding is so severe that the varices cannot be seen. Band ligation of the varices is another way of treatment.
 - iii. *Vasoconstrictor therapy:* Temporary control is achieved by vasopressin, 20 units are given in 100 c.c. of 5 percent dextrose intravenous over ten minutes then 0.4 unit per minute is started for maximum of two hours. One should monitor BP and be careful about any coronary vasospasm which may occur. Vasopressin acts by decreasing splanchnic blood flow and portal pressure. This drug is tapered and discontinued after 48 hours. Octreotide (somatostatin analogue) IV 50 micrograms bolus followed by an infusion of 50 micrograms per hour for 48 hours produce splanchnic vasoconstriction without any systemic side effects. It should be used as first line drug while awaiting sclerotherapy because of lesser side effects.
 - iv. *Sengstaken-Blakemore tube:* This may be inserted in the stomach and inflated and attached to traction to provide local compression of the sub-mucosal veins. Important complications include discomfort to the patient, rebleeding, esophageal ulceration, airway obstruction or aspiration.

- v. *Transhepatic catheterization and occlusion:* Occlusion of the left gastric vein may result in cessation of bleeding.
- vi. *Surgical:* Shunting procedures are required to arrest the bleeding and they may be performed within a few days. Mortality is 25 to 50 percent. Elective shunt surgery may be required, but it does not prolong longevity. It does, however, prevent recurrent variceal haemorrhage. The type of shunt, i.e. portacaval or splenorenal depends upon the judgement of the surgeon according to the patient's condition and Child-Pugh classification of the patient.

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C A S E

Amoebic Liver Abscess

BRIEF HISTORY

A 45-year-old man presented to the accident and emergency department with one-week history of high grade fever and rigors accompanied by profuse sweating. He had noticed undue weakness and loss of appetite. Most of the time he felt nauseated and vomited on couple of times. Four weeks prior to present condition, he developed loose motions with occasional blood and mucus in the stools, but it settled after some medications from the doctor. He complained of pain in the abdomen which was more marked on the right side. He had been well in the past apart from occasional attacks of bronchitis. He smoked 20 to 25 cigarettes per day. There was no family history of any disease.

IMPORTANT CLUES ON CLINICAL EXAMINATION

On examination, he looked toxic. Temperature was 104°F. Pulse was 130 per minute and regular. BP was 120/80 mmHg. Abdominal examination revealed mild tenderness in the right hypochondrium and liver was just palpable. Spleen was not enlarged and bowel sounds were present. Rectal examination was normal. Cardio-vascular, respiratory and neurological examinations were normal.

INVESTIGATIONS

Following investigations were ordered:

Hb:	13.4 g/dl (normocytic normochromic)	Blood urea:	8 mmol/l (48 mg/dl)
		Blood sugar:	6 mmol/l (108 mg/dl)
		Creatinine:	1.2 umol/l (1.2 mg/dl)
WCC:	15.4 × 10 ⁹ /l	Urine:	normal

Contd...

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	P:84% L:12% M:3% E:1%	ECG:	sinus tachycardia with occasional ventricular ectopics.
Platelets:	$340 \times 10^9/l$		
ESR:	45 mm in 1st hour	Chest X-ray:	normal lung and cardiac shadow, slightly raised right dome of the dia- phragm.
Sodium:	140 mmol/l		
Potassium:	4.5 mmol/l		
Bicarbonate:	26 mmol/l		
Chloride:	101 mmol/l		

QUESTIONS

- Q.1. What is the most likely diagnosis?
- Q.2. What is the differential diagnosis?
- Q.3. What further investigations are required?
- Q.4. What treatment can be offered?

ANSWERS

- A.1.** In a patient with a previous history of loose motions with mucus and blood (intestinal amoebiasis) and now development of high grade fever with rigours, pain in the right upper quadrant of abdomen with malaise and evidence of leukocytosis with raised polymorphonuclear leukocytes indicate development of a liver abscess, most probably, amoebic.
- A.2.** This should be differentiated from:
- i. Acute appendicitis
 - ii. Acute cholecystitis
 - iii. Perforated ulcer
 - iv. Acute pancreatitis.
- A.3.** This includes:
- i. Liver function tests, serum amylase.
 - ii. Abdominal ultrasound.
 - iii. Serological tests for amoebiasis.
 - iv. CT scan.
 - v. Radio-isotope liver scan.
 - vi. Ultrasound guided needle aspiration results in the withdrawal of pus which is typically described as anchovy sauce. There are no polymorphs or amoeba. Parasites are usually localized in the wall and are usually demonstrated in the terminal portion of the aspirate.
- A.4.** Few medicines can be used for hepatic amoebiasis:
- i. Chloroquine disphosphate is useful because of its high concentration in the liver.
 - ii. Emetine was used in the past and was quite effective, but due to its potential cardiotoxicity, it is now out of fashion.
 - iii. Metronidazole (Flagyl) is unique as it is both effective and safe and is given in high doses, i.e., 800 mg thrice a day for 5 to 10 days.
- Hepatic amoebiasis is still accompanied by quite high mortality but exact figures are not available.

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C A S E

Malabsorption

BRIEF HISTORY

A 62-year-old woman was admitted with eight-week history of diarrhoea, weight loss, tiredness and lethargy. She denied having any abdominal pain or vomiting, but admitted that she had lost about 7 kg of weight. Diarrhoea was in the form of 3 to 5 loose motions a day without blood or mucus. The colour of faeces was pale, and she had noticed at times that she had to flush the toilet repeatedly, since the stools either floated or tended to stick to the closet. At times, they were foul smelling too. She had always been fit. There was no past history of such an illness, diabetes or hypertension.

IMPORTANT CLUES ON CLINICAL EXAMINATION

On examination, she looked pale. JVP was not raised, but she had pitting oedema on both feet. There was no clubbing, lymphadenopathy or jaundice. Blood pressure was 145/85 mmHg, and pulse was 80 per minute and regular. The thyroid gland was enlarged, but clinically she was euthyroid. In the abdomen there were no scars. Liver and spleen were not enlarged. Examinations of respiratory, cardiovascular and nervous system were normal.

INVESTIGATIONS

Following investigations were available:

Hb:	8.5 g/dl (macrocytic normochromic)	Blood sugar:	7.4 mmol/l (133 mg/dl)
		Total protein:	5.7 g/dl
		Albumin:	3.2 g/dl
WCC:	$9 \times 10^9/l$	Alk.phos:	280 u/l

Contd...

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	P:72% L:24%	Serum folate:	25 ug/l (normal 3-12 ug/l)
	M:3% E:1%	RBC folate:	800 ug/l (normal 160-640 ug/l)
MVC:	102fl		
Platelets:	$267 \times 10^9/l$	Serum B ₁₂ :	70 ug/l (normal 150-900 ug/l)
ESR:	23 mm in 1st hour	Urine:	normal
Sodium:	137 mmol/l	Faecal fat:	10 g/24 hrs (normal less than 6 g/24 hours)
Potassium:	4.2 mmol/l		
Bicarbonate:	25 mmol/l		
Chloride:	99 mmol/l		
Calcium:	2.6 mmol/l (10.4 mg/dl)		
Blood urea:	8 mmol/l (48 mg/dl)		
Creatinine:	97umol/l (1.9 mg/dl)		

QUESTIONS

- Q.1.** What is the most likely diagnosis?
- Q.2.** What is this due to?
- Q.3.** What is the relation between this condition and blind loop syndrome?
- Q.4.** Give four investigations which can help in the diagnosis.
- Q.5.** List a few causes of your final diagnosis.

ANSWERS

- A.1.** In a patient with history of loose motions, pale stools, which are difficult to flush and laboratory findings of macrocytic anaemia, low serum B₁₂ and high 24 hour faecal fat favours strongly a diagnosis of malabsorption.
- A.2.** This is due to blind loop syndrome as the finding of low B₁₂ with a normal folate level further points towards the underlying cause being a blind loop syndrome resulting in stasis and bacterial colonisation. Previous gastric or intestinal surgery, duodenal or jejunal diverticuli and diabetes mellitus are common causes for such blind loop syndrome. In old age, sometimes, the blind loop syndrome may be seen without any obvious anatomical changes.
- A.3.** Passage of excessive fats in stools is called steatorrhea. Bacterial overgrowth in the blind loop causes deconjugation of bile salts which are required for fat absorption. Non-availability of bile salts interferes with fat absorption. Further, disconjugated bile salts act as irritants in the large gut and result in diarrhoea.
- A.4.**
- i. Barium meal and follow through: May show diverticulae or increased flocculation of barium.
 - ii. 14-C labelled glycocholic acid test: This is based on the ability of intestinal bacteria to disconjugate bile acids. Results are expressed as percentage of 14C excreted divided by CO₂ trapped, then multiplied by body weight. In normal subjects values in each of the first 3 hours are below 0.1 percent and no value exceeds 0.3 percent. In upper small bowel, bacterial overgrowth values from 2 hours are raised with maximal values at 3 to 5 hours. In intestinal hurry, normal colonic bacteria may give late positive results.
 - iii. Urinary indican: There is increased excretion of this substance in the urine. Normal urinary indican excretion is 48 ± 20 mg/24 hours. Values above 80 mg/24 hours imply profuse bacterial proliferation.
 - iv. Upper G.I. endoscopy and duodenal and jejunal biopsy and intubation and aspiration of contents and their analysis may also help in this diagnosis.

A.5. The causes of malabsorption can be classified as follows:

A. *Mucosal defects:*

- i. Celiac disease (gluten, cow's milk, soya protein)
- ii. Whipple's disease.
- iii. Intestinal lymphangiectasia.
- iv. Alactasia.
- v. Abetalipoproteinaemia.

B. *Structural defects:*

- i. Crohn's disease.
- ii. Resection of bowel or stomach.
- iii. Mesenteric insufficiency.
- iv. Lymphoma.

C. *Infective causes:*

- i. Acute enteritis.
- ii. Traveller's diarrhoea.
- iii. Parasitic disease.
- iv. Hypogammaglobulinaemia.

D. *Defective luminal digestion:*

- i. Parenchymal liver disease.
- ii. Pancreatic insufficiency.
- iii. Cystic fibrosis.
- iv. Zollinger-Ellison syndrome.

E. *Drugs:*

- i. Neomycin.
- ii. PAS.
- iii. Metformin.
- iv. Methotrexate.
- v. Antacids.

F. *Miscellaneous:*

- i. Congenital lymphangiectasia.
- ii. Hyperthyroidism.
- iii. Carcinoid syndrome.
- iv. Enterokinase deficiency.
- v. Disaccharidase deficiency.

Hepatic Encephalopathy

BRIEF HISTORY

A 45-year-old male was brought to accident and emergency department after a severe bout of haemoptysis and sudden deterioration in the level of consciousness. The brother mentioned that a year ago he had jaundice which lasted for about a month and then he took some medicines from Hakims and got a bit better but continued to have malaise, increased tiredness and easy fatigueability. The patient had also noticed that his abdomen was bloating and legs were swelling up, too. One week prior to this, he vomitted blackish fluid. His wife had noticed that for the last few days, he was becoming increasingly sleepy and behaved in a strange way. He was also becoming forgetful and irritable. There was no history of recent drug intake, but he was taking laxative more often without much success. He was not a known diabetic or hypertensive.

IMPORTANT CLUES ON CLINICAL EXAMINATION

On examination, he looked pale and was very drowsy and responded only to painful stimuli. He had mild jaundice. There was no clubbing, cyanosis or lymphadenopathy. Poedal oedema was noticed. His pulse was 130 per minute and regular. BP was 105/65 mm Hg. Cardiovascular and respiratory systems were normal. Abdominal examination showed tenderness in the epigastrium, liver was not palpable, spleen was just palpable and there was moderate ascites. There were no signs of meningeal irritation, but the reflexes were exaggerated with upgoing plantars.

INVESTIGATIONS

Following were the investigations carried out:

Hb:	8.4 g/dl (hypochromic macrocytic)	Blood sugar:	5.5 mmol/l(99 mg/dl)
		Serum bilirubin:	34 ummol/l (2 mg/dl)
WCC:	10.2 × 10 ⁹ /l P:78% L:16% M:4% E:2%	SGOT (AST):	48 U/l
		SGPT (ALT):	40 U/l
Platelets:	240 × 10 ⁹ /l	Total proteins:	6.8 g/dl
ESR:	46 mm in 1st hour	Albumin:	2.4 g/dl
		Alk. phos:	200 U/l
Sodium:	142 mmol/l	Urine:	normal
Potassium:	3.8 mmol/l	ECG:	no evidence of myocardial infarction
Bicarbonate:	24 mmol/l	Chest X-ray:	normal
Chloride:	99 mmol/l		
Blood urea:	10 mmol/l (60 mg/dl)		
Creatinine:	143 umol/l (1.6 mg/dl)		

QUESTIONS

- Q.1. What is the most likely diagnosis?
- Q.2. What is the differential diagnosis?
- Q.3. What further investigations may be of help?
- Q.4. What is asterixis? In what conditions is it present?
- Q.5. Briefly outline the management and discuss a little about lactulose (duphalac).

ANSWERS

- A.1.** In this patient who is known to have some liver problems in the past and now presents with haematemesis and is semicomatosed, the most likely diagnosis is hepatic encephalopathy.
- A.2.**
- i. Hyponatraemia.
 - ii. Acute alcoholism.
 - iii. Psychiatric disorders.
- A.3.**
- i. *Lumbar puncture*: There may be increased CSF protein but cell count is normal. Glumatic acid and glutamine may be increased.
 - ii. *Electroencephalogram (EEG)*: There is slowing of the frequency from the normal alpha range of 8 to 13 cps (cycles per second) to the delta range of below 4 cps.
- A.4.** This is also called flapping tremors and occur due to impaired inflow at joints and other afferent information to the brain-stem reticular formation. It is also caused by renal and respiratory failure besides hepatic encephalopathy.
- A.5.** This can be as follows:
- i. Acute precipitating factors should be identified and dealt with properly, e.g., haemorrhage, infection, electrolyte imbalance, i.e., hypokalaemie, sedatives and large protein meals.
 - ii. Empty bowels with enemata and lactulose.
 - iii. Give protein free diet.
 - iv. Antibiotics—Neomycin—1 gram 6 hourly orally for one week.
 - v. Maintain calories, fluid and electrolyte balance.
 - vi. Stop diuretics and check electrolyte levels regularly.
 - vii. Consider trial of flumazenil (Annexate) a benzodiazepine antagonist which can cause temporary arousal in acute hepatic encephalopathy.

Lactulose acts by different mechanisms:

The first is that it changes the growth environment of the ammonia producing organisms by increasing the population of lactose-fermenting bacteria, therefore, no ammonia is produced and there is no neurotoxicity.

Secondly, lactulose, which is not absorbed from intestine, acts as osmotic diarrhoeal agent and flushes away the bacteria which may or may not be ammonia producing. But the first mode of action is far better.

Thirdly, it converts ammonia in the intestine to ammonium ion by incorporating H^+ which is not neurotoxic.

N.B: Grades of Hepathic Encephalopathy:

- Grade 1: Confused, altered mood and behaviour, psychometric defects.
- Grade 2: Drowsy, inappropriate behaviour.
- Grade 3: Stuporous but speaking and obeying simple commands, inarticulate speech, marked confusion.
- Grade 4: Coma.
- Grade 5: Deep coma and no response to painful stimuli leading to death.

Constipation

BRIEF HISTORY

A 58-year-old woman was admitted with a history of frequency of micturition for two days. She had also suffered from severe osteoarthritis mainly affecting her knees and left hip for which she was taking, paracetamol regularly for the last two years. For the last three weeks, she was started on some “stronger” pain killers since paracetamol was not enough to control her pain. Because of her increasing pain, she had been getting depressed for the last six months and had become almost housebound. She used to cry and complained of insomnia and took sleeping pills. She was not a known hypertensive or diabetic.

IMPORTANT CLUES ON CLINICAL EXAMINATION

On examination, she looked depressed and was mildly confused. JVP was not raised. Blood pressure was 140/70 mmHg. Pulse was regular. Thyroid and lymph nodes were not enlarged. There was no clubbing, oedema or jaundice. She had painful limitation of movements of both her knees and left hip. Her abdomen was distended and soft masses could be palpated all along the left side of it. Bowel sounds were rather more active. On rectal examination, she was impacted and a finger was stained with soft faeces and mucus but no blood.

Examinations of the cardiovascular and respiratory systems were normal. There were no localising neurological signs except she had small sized pupils.

INVESTIGATIONS

Following results of investigations were available:

Hb:	13 g/dl (normocytic normochromic)	Chloride:	92 mmol/l
		Blood urea:	12 mmol/l (72 mg/dl)
WCC:	$6.7 \times 10^9/l$ P:72% L:24% M:4% E:2%	Creatinine:	140 $\mu\text{mol/l}$ (1.6 mg/dl)
		Blood sugar:	6.2 mmol/l (112 mg/dl)
Platelets:	$370 \times 10^9/l$	Urine:	normal
ESR:	28 mm in 1st hour	ECG:	heart size normal lung fields were clear.
Sodium:	142 mmol/l	Chest X-ray:	normal
Potassium:	3.3 mmol/l		
Bicarbonate:	25 mmol/l		

QUESTIONS

- Q.1.** What factors are responsible for this patient's faecal impaction?
- Q.2.** Name four other drugs which commonly cause this problem.
- Q.3.** Give five complications of this condition.
- Q.4.** What is the cause of urinary incontinence in this patient?
- Q.5.** What treatment can be offered?
- Q.6.** What metabolic conditions may precipitate this condition?

ANSWERS

- A.1.** This patient has had poor mobility due to arthritis and was started on “stronger” medicines, probably, containing opiates to control arthritis. Opiates derivatives are well recognised to cause constipation. Furthermore, she was depressed and taking some antidepressant drugs which can cause constipation leading to faecal impaction. This problem is more in Western societies where they take less roughage.
- A.2.**
- i. Oral iron therapy.
 - ii. Antidepressant-tricyclic group.
 - iii. Antiparkinsonian drugs especially anticholinergic drugs.
 - iv. Diuretics causing dehydration.
- A.3.**
- i. Irritability and confusional state.
 - ii. Faecal incontinence—also called spurious diarrhoea or overflow incontinence.
 - iii. Obstruction—may be complete or partial, complete is called obstipation when there is neither passage of faeces nor flatus.
 - iv. Stercoral ulceration—due to impaction of hard faeces on the rectosigmoid mucosa.
 - v. Megacolon—if the colon is distended with gases and become atonic.
- A.4.** When rectosigmoid colon is loaded with faeces, it compresses the urethra and the urinary bladder and either cause retention of urine or frequency of micturition. This is more common in the aged people.
- A.5.** Regular mobility and change in dietary habits help a lot, especially high fibre diet, i.e. green vegetables and unprocessed cereal grains or bran. Regular administration of stool softener, bulk laxatives or mild cathartics are also required. In some cases, enemata may also be used.
- A.6.** There are a few metabolic abnormalities such as:
- i. Hypothyroidism
 - ii. Hypercalcaemia
 - iii. Hypokalaemia
 - iv. Porphyrria
 - v. Lead poisoning.

Intestinal Obstruction

BRIEF HISTORY

A 68-year-old woman presented to the accident and emergency department with a two-day history of generalized abdominal pain which was followed by vomiting for twenty hours before admission. She had no fever, cough, expectoration, chest pain or palpitation. There were no urinary symptoms, but she had no bowel action for the last five days and was passing no wind or faeces per rectum. She was not a diabetic or hypertensive, but had a history of osteoarthritis and parkinsonism for which she was on a few medicines.

IMPORTANT CLUES ON CLINICAL EXAMINATION

On examination, she was dehydrated and kyphoscoliosis was obvious. Blood pressure was 140/60 mmHg. Pulse was 88 per minute and regular. There was no clubbing, anaemia, thyroid swelling or lymph node enlargement. She was mildly confused and could not remember her own address. Abdomen was distended with some irregular mass in the left iliac fossa along the descending colon. Bowel sounds were faintly audible. Rectal examination confirmed the presence a large amount of faeces. No masses were palpable and the finger was not blood stained. She had rest tremors and some rigidity in her limb, but could walk without any difficulty.

INVESTIGATIONS

Following were the results of various investigations:

Hb:	14 g/dl	Blood urea:	12 mmol/l (72.6 mg/dl)
	(normocytic	Creatinine:	140 umol/l (1.6 mg/dl)
	normochromic)	Blood sugar:	9 mmol/l (162 mg/dl)

Contd...

Contd...

WBC:	$8 \times 10^9/l$	Urine:	normal
	P:79% L:16%	ECG:	normal sinus rhythm
	M:3% E:2%	X-ray chest:	norml heart size;
ESR:	34 mm in 1st hour		no lung lesions seen
Sodium:	145 mmol/l	X-ray	as shown in Figure 24.1
Potassium:	4.6 mmol/l	abdomen:	
Bicarbonate:	26 mmol/l		
Chloride:	101 mmol/l		

**Fig. 24.1****QUESTIONS**

- Q.1.** What is the most likely diagnosis?
- Q.2.** Give salient features if large bowel is involved.
- Q.3.** How many fluid levels are normal on an erect plain abdominal X-ray film?
- Q.4.** What is obstipation?

ANSWERS

- A.1.** The most likely diagnosis in this lady with constipation, faecal impaction, abdominal pain and vomiting with fluid levels on erect abdominal film is intestinal obstruction which has, probably, been caused by the faecal impaction. Constipation is comparatively uncommon but is a recognised cause of large bowel obstruction specially in the elderly, who do not take a reasonable amount of roughage and fluids.
- A.2.** In contrast to small bowel obstruction, constipation lasting for days or weeks is the predominant feature followed by abdominal distension specially in the flanks. Pain in large intestinal obstruction is usually more diffused, dull and continuous but may come in the form of colic usually in the hypogastric region. It is not uncommon for vomiting to be delayed for two to three days. Plain abdominal X-ray may or may not show the fluid levels. The larger the number of fluid levels, the nearer the obstruction is to the ileocaecal valve.
- A.3.** Three:
- First in the stomach.
 - Second at the duodenojejunal junction.
 - Third at the ileocaecal region.
- A.4.** When there is no passage of flatus or faeces per rectum then, it is called absolute constipation or obstipation.

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C A S E

Mesenteric Infarction

BRIEF HISTORY

A man of 73 was admitted with a two-hour history of sudden severe central abdominal pain, vomiting and diarrhoea. There was no history of haematemesis or malaena. He was known to suffer from ischaemic heart disease, atrial fibrillation and diabetes mellitus. His diabetes had been well controlled on oral hypoglycaemic agents. Other drugs included isordil and digoxin. On the day of this pain, he had taken his usual food and tablets. There was no history of headaches, fits or faints.

IMPORTANT CLUES ON CLINICAL EXAMINATION

On examination, he was in pain and sweaty over forehead. Blood pressure was 110/70 mmHg. Pulse 84 per minute and irregular. Thyroid and lymph nodes were not enlarged. No anaemia, clubbing or cyanosis was noticed. His pulse was mightily irregular with an apical rate of 100 per minute and had soft systolic apical murmur. Respiratory system was normal. In the abdomen, he had diffuse periumbilical tenderness but no guarding or rebound tenderness was noticed. Bowel sounds were faintly audible. Rectal examination was normal. Examination of nervous system was unremarkable.

INVESTIGATIONS

Following were the results of various investigations:

Hb:	13.4 g/dl	Creatinine:	270 umol/l (3.0 mg/dl)
	(normocytic	Protein:	7.2 g/dl
	normochromic)	Albumin:	3.6 g/dl

Contd...

Contd...

WCC:	11 × 10 ⁹ /l P 72% L 20% M 4% E 4%	Bilirubin:	17 umol/l(0.9 mg/dl)
		Urine:	normal
		Serum	396 iu/l
Platelets:	350 × 10 ⁹ /l	amylase:	
ESR:	39 mm in 1st hour	Chest X-ray:	heart size slightly enlarged.
Sodium:	135 mmol/l	X-ray	no fluid levels or air
Potassium:	3.6 mmol/l	abdomen:	under the diaphragm
Bicarbonate:	24 mmol/l	ECG:	atrial fibrillation,
Chloride:	100 mmol/l		no acute changes of
Blood glucose:	7.8 mmol/l (140 mg/dl)		myocardial infarction.
Blood urea:	36 mmol/l (216 mg/l)		

QUESTIONS

- Q.1. What is the most likely diagnosis?
- Q.2. How would you confirm your diagnosis?
- Q.3. What are the radiological characteristics of this disease?
- Q.4. Why is serum amylase raised?

ANSWERS

- A.1.** The most likely diagnosis in this elderly man is mesenteric infarction. The patient suffers from atrial fibrillation, ischaemic heart disease and diabetes mellitus and this may have been caused by thromboembolism due to uncontrolled atrial fibrillation because there was no ECG changes of myocardial infarction. The onset was sudden with abdominal pain, vomiting, diarrhoea and atrial fibrillation, should always raise the possibility of such complication.
- A.2.** The ultimate confirmation in such a patient with an acute abdomen (with no evidence of diabetic ketoacidosis) can be done only by emergency laparotomy. In fact, on laparotomy this patient was found to have loops of gangrenous bowel.
- A.3.** In case of ischaemic colitis, if a barium enema is performed, then there is classical appearance called thumb printing on X-ray as shown in Figure 25.1.

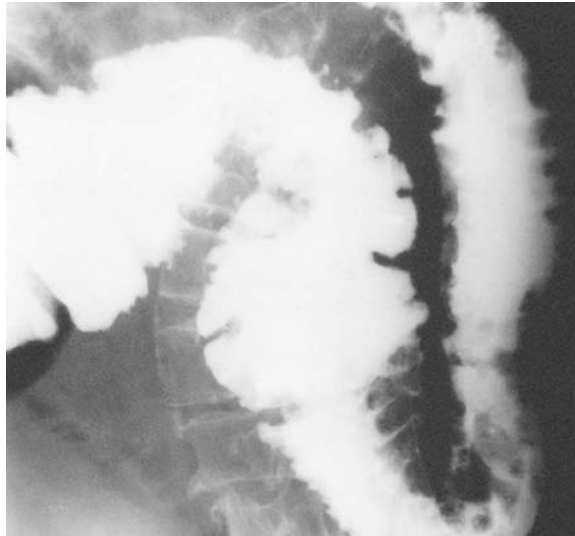


Fig. 25.1

- A.4.** In mesenteric infarction, serum amylase is raised, but there is no evidence of acute pancreatitis. This should always be remembered as both acute pancreatitis and mesenteric infarction can cause rise in serum amylase.

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C A S E

Ulcerative Colitis

BRIEF HISTORY

A 27-year-old man presented to the accident and emergency department with a history of passage of loose motions for the last two days. The stools he was passing were mixed with blood and mucus and were about 10 to 12 per day. He also mentioned about fever and abdominal discomfort. There was no history of drug intake and on further questioning he told that he had been passing loose motions off and on for the last two months and they were sometimes containing mucus and blood for which he took medicine from his doctor but never had such an attack before. One of his uncles also had similar problems but ultimately died of heart attack.

IMPORTANT CLUES ON CLINICAL EXAMINATION

On examination, he looked toxic, dehydrated, anaemic and wasted. Temperature was 102°F. Pulse was 120 per minute regular and all pulses were palpable. BP was 110/70 mmHg. Heart sounds were of normal intensity with an ejection systolic murmur at aortic area. There was minimal pitting oedema. Chest was clear. Abdomen was distended and tympanitic. It was tender in left iliac fossa. No viscera were palpable. Rectal examination by the finger showed blood and mucus.

INVESTIGATIONS

Investigations included:

Hb:	7.8 g/dl	Potassium:	3.8 mmol/l
	(microcytic	Bicarbonate:	24 mmol/l
	hypochromic with	Chloride:	98 mmol/l
	few tear drop cells)	Urine:	normal

Contd...

Contd...

WBC:	14.5 × 10 ⁹ /l	ECG:	sinus tachycardia
	P:82% L:14%	X-ray Abd:	large bowel
	M:2% E:2%		distended with
ESR:	86 mm in 1st hour		width more than
Sodium::	140 mmol/l		7.5 cm across

QUESTIONS

- Q.1. What is the diagnosis?
- Q.2. What further investigations would you ask for?
- Q.3. Is the X-ray abdomen significant?
- Q.4. What is the differential diagnosis?
- Q.5. What are the complications?
- Q.6. How would you manage such a case?

ANSWERS

- A.1.** A young male with a history of loose motions in the past and now presenting with 10 to 12 motions a day with blood and mucus and toxic look with distended and tender abdomen favours a diagnosis of ulcerative colitis more strongly than any other inflammatory bowel diseases.
- A.2.**
- i. *Blood culture:* At least two or three sets of blood cultures are important though they may be negative.
 - ii. *Stool examination:* It is important to rule out an infective dysentery. Cultures are also required.
 - iii. *Sigmoidoscopy and biopsy:* Currently, facilities of flexible sigmoidoscopy are available therefore, it can be performed. The mucosa looks uniformly inflamed, oedematous, friable with contact bleeding and ulceration which is a typical finding of acute attack of ulcerative colitis. Biopsy will confirm the diagnosis.
 - iv. *Barium enema:* It should not be performed in acute setting but after a few weeks or months when in remission.
- A.3.** Yes. The dimensions of the large bowel indicate that the patient has developed toxic megacolon which if not managed urgently, can perforate leading to acute peritonitis.
- A.4.** It should be differentiated from Crohn's colitis, pseudo-membranous enterocolitis, ischaemic colitis, amoebic dysentery, campylobacter colitis, carcinoma colon, villous adenoma, etc.
- A.5.** These can be divided into:
- A. *Nutritional deficiencies*
 - Anaemia
 - Vitamin deficiencies
 - Dehydration
 - Hypokalaemia
 - Hypoproteinaemia
 - B. *Colonic*
 - Acute toxic dilatation
 - Perforation
 - Massive haemorrhage

- Crypt abscesses
- Carcinoma
- Stricture
- Pericolic abscess.
- C. *Anal*
 - Haemorrhoids
 - Anal fissure
 - Anal fistula
 - Perianal abscess
- D. *Ectodermal*
 - Aphthous ulcers
 - Clubbing
 - Erythema nodosum
 - Erythema multiforme
 - Pyoderma gangrenosum
- E. *Arthritis*
 - Polyarthritis
 - Sacroiliitis
 - Ankylosing spondylitis
- F. *Ocular*
 - Uveitis
 - Episcleritis
 - Keratitis
 - Retinitis
 - Retrobulbar neuritis
- G. *Hepatic*
 - Fatty infiltration
 - Granulomata
 - Focal necrosis
 - Abscess
 - Cirrhosis
 - Pericholangitis
 - Sclerosing cholangitis
 - Portal pyaemia
- H. *Renal*
 - Pyelonephritis
 - Calculi
- I. *Thrombophlebitis*
- J. *Iatrogenic*
 - Drugs

Transfusions

Surgery, etc.

A.6. The management can be divided into medical and surgical and also depends upon the severity of the attack. Besides this, supportive therapy is also significant which include:

- Symptomatic therapy
- Diet
- Nutritional therapy
- Iron therapy

A. *Mild attack (Stool frequency less than four/day)*

- Asacol 1 gram four times daily
- Steroid enema at night (100 mg hydrocortisone)
- Relieve proximal faecal stasis.

B. *Moderate attack (Stool frequency more than six/day)*

- Steroid enema once or twice a day
- Asacol 1 gram two to four times a day
- Oral prednisolone 40 mg daily.

C. *Severe attack (Stool frequency more than twelve/day) (Trulove regimen)*

- Urgent hospitalization, daily electrolytes
- Blood transfusion, IV fluids, parenteral nutrition
- Nil by mouth
- Hydrocortisone parenterally
- Steroid enema twice daily—Predfoam enemas are better tolerated, easily administered and contact with inflamed rectal/colonic mucosa is longer than fluid enemata.
- Metronidazole

Surgical management

Indications for surgery in ulcerative colitis.

These can be divided into:

A. *Emergency indications*

- i. Perforation (Proven or suspected)
- ii. Toxic dilatation
- iii. Failed medical treatment
- iv. Massive haemorrhage.

B. *Elective indications*

- i. Failed medical treatment (chronic ill health)
- ii. Suspected carcinoma

- iii. Risk of carcinoma
 - iv. Growth retardation
 - v. Infantilism
 - vi. Systemic (e.g., arthritis, uveitis, pyoderma gangrenosum)
 - vii. Pelvic (e.g., rectovaginal fistula).
- Surgical procedures include proctocolectomy with an ileostomy. Colectomy with an ileorectal or ileo-ileal anastomosis is used to avoid ileostomy.

Acute Pancreatitis

BRIEF HISTORY

A 39-year-old woman was brought to the accident and emergency department with a history of severe epigastric pain, vomiting and fever for one day. There was no history of malaena or haemetemesis. She had complained of mild epigastric discomfort especially after fatty meals and used antacids and carminatives which relieved her symptoms temporarily. She was not a known diabetic or hypertensive. One of her cousins had died of a heart attack recently, otherwise there was nothing else significant in the family history. No allergies were noticed.

IMPORTANT CLUES ON CLINICAL EXAMINATION

On examination, she was restless and had sweating on her forehead. Temperature was 99.4°F. Pulse was 120 per minute and regular, and BP was recorded at 90/60 mmHg. She looked to have mild jaundice. Cardiovascular system was normal, while respiratory system showed decreased breath sounds on right side at the base. Abdominal examination showed tender epigastrium but no masses or viscera were palpable. Neurological examination was unremarkable.

INVESTIGATIONS

Investigations included:

Hb:	13.2 g/dl	Urea:	6.8 mmol/l (41 mg/dl)
	(normocytic	Creatinine:	117 umol (1.3 mg/dl)
	normochromic)	Bilirubin:	34 umol/l (2.0 mg/dl)

Contd...

Contd...

WBC:	12.4 × 10 ⁹ /l	SGOT(AST):	39 U/l
	P:80% L:16%	SGPT (ALT):	39 U/l
	M:2% E:2%	Alk phos:	176 U/l
ESR:	45 mm in	Serum amylase:	400 U/l
	1st hour	Urine:	glucose ++
Platelets:	295 10 ⁹ /l	Chest X-ray:	small right-sided
Sodium:	140 mmol/l		pleural effusion.
Potassium:	4.3 mmol/l	ECG:	sinus tachycardia, no
Bicarbonate:	25 mmol/l		ischaemic changes
Chloride:	110 mmol/l		
Blood sugar:	11.6 mmol/l		
	(209 mg/dl)		

QUESTIONS

- Q.1. What is the diagnosis?
- Q.2. What is the differential diagnosis?
- Q.3. List a few causes of this disease.
- Q.4. List complications of this disease.
- Q.5. What are the specific "signs" associated with this disease?
- Q.6. Describe management of your final diagnosis.

ANSWERS

A.1. In a patient with a previous history of indigestion and intolerance to fatty food and presentation as severe epigastric pain leading to shock with a high amylase and mildly derranged LFT's with leucocytosis point to a diagnosis of acute pancreatitis.

A.2. This includes:

- i. Perforated viscus especially peptic ulcer.
- ii. Acute cholecystitis and biliary colic.
- iii. Acute intestinal obstruction.
- iv. Renal colic.
- v. Myocardial infarction.
- vi. Mesenteric vein thrombosis.
- vii. Dissecting aortic aneurysm.
- ix. Pneumonia.
- x. Diabetic ketoacidosis.

A.3. These can be classified as follows:

- i. Alcohol.
- ii. Gallstones.
- iii. Post endoscopic procedure, e.g. (ERCP).
- iv. Blunt trauma.
- v. Metabolic causes, e.g. hyperlipidaemia, hyperparathyroidism.
- vi. Hereditary pancreatitis.
- vii. Infections, e.g. mumps, viral hepatitis, ascariasis, mycoplasma.
- viii. Drug induced, e.g. thiazide diuretics, anti-inflammatory drug, antimicrobials, oral contraceptives, etc.
- ix. Connective tissue disorders, e.g. SLE, angitis, thrombotic thrombocytopaenic purpura.
- x. Penetrating duodenal ulcer.
- xi. Obstruction at ampulla of Vater.

A.4. They are classified as follows:

- A. *Local*
 - i. Phlegmon and pancreatic abscess.
 - ii. Pancreatic pseudocyst and its complications, e.g., pain, rupture, infection, haemorrhage.
 - iii. Pancreatic ascites (rich in amylase).
 - iv. Bowel infarction, and thrombosis of blood vessels.
 - v. Obstructive jaundice.

B. *Systemic*

- i. Pulmonary, e.g. pleural effusion, atelectasis, mediastinal abscess, pneumonitis, and adult respiratory distress syndrome (ARDS).
- ii. Cardiovascular, e.g. hypotension, sudden death, nonspecific ST-T changes, pericardial effusion.
- iii. Haematologic, e.g. disseminated intravascular coagulation (DIC).
- iv. Gastro-intestinal haemorrhage, e.g. peptic ulcer, erosive gastritis, haemorrhagic pancreatitis, portal vein thrombosis, and variceal haemorrhage.
- v. Renal, e.g. oliguria, azotemia, renal artery or vein thrombosis.
- vi. Metabolic, e.g. hyperglycaemia, and hypertriglyceridaemia, hypocalcaemia.
- vii. Central nervous system, e.g. psychoses, and fat emboli.
- viii. Fat necrosis in subcutaneous tissue, bone, miscellaneous, i.e. (pleura, mediastinum, CNS).
- ix. Hepatic, e.g. jaundice, and portal vein thrombus.

A.5. *Cullen's sign*: It is a faint blue discolouration around the umbilicus which may occur as a result of haemoperitoneum.

Grey-Turner's sign: It is a bluish red or greenish brown discolouration of the flanks which reflects tissue catabolism of haemoglobin. Both the above mentioned signs indicate the presence of a severe necrotizing pancreatitis.

A.6. In 80 to 90 percent of patients with acute pancreatitis, the disease is self limiting within 2 to 5 days. Medical treatment mostly consists of reducing pancreatic secretions and putting pancreas at rest. These include:

- i. Analgesics for pain.
- ii. Intravenous fluids to keep normal intravascular volume.
- iii. No oral alimentation.
- iv. Nasogastric suction to decrease gastric secretions.
- v. Antibiotic therapy for established infection.
- vi. Aprotinin (Trasylol) and glucagon have not proved effective in some studies. Somatostatin infusions have been disappointing, too.
- vii. Fulminant pancreatitis requires laparotomy and peritoneal lavage.

Carcinoma Colon

BRIEF HISTORY

A 65-year-old gentleman attended the outpatient clinic with a history of increased breathlessness, swelling of feet, easy fatigueability and weight loss for about two months. His appetite was moderate and there was no history of any drug intake. He also complained of pain in the chest on exertion which subsided after taking rest. For the last three months, he had noticed some change in his bowel movement. He had occasional diarrhoea and sometimes constipation. He also noticed that for the last four weeks, his piles were troubling him more in the way of bleeding. He stopped smoking about five years back. One of his uncles died of cancer of stomach.

IMPORTANT CLUES ON CLINICAL EXAMINATION

On examination, he looked a bit anxious. Pallor was obvious, but there was no jaundice. Minimal pitting oedema of both feet was noticed. Pulse was 100 per minute and BP was 149/90 mmHg. Auscultation of precordium revealed an ejection systolic murmur. Respiratory system was unremarkable. On abdominal examination, descending colon was palpable and was loaded, probably, with faeces. Liver or spleen was not palpable and there was no ascites. Two haemorrhoids of second degree were present.

INVESTIGATIONS

Investigations revealed:

Hb:	6.9 g/dl	Bicarbonate:	29 mmol/l
	Microcytic	Urine:	normal
	hypochromic	Liver function	
	with pencil and	tests:	normal
	tear drop cells.	Chest X-ray:	normal lung marking

Contd...

Contd...

WBC:	8.4 × 10 ⁹ /l	ECG:	and heart size
	P:72% L:26%		sinus rhythm, T-wave
	M:1% E:1%		inverted in lateral
Platelets:	580 × 10 ⁹ /l		chest leads.
ESR:	89 mm in 1st hour		
Sodium:	134 mmol/l		
Potassium:	5.6 mmol/l		

QUESTIONS

- Q.1. What is the diagnosis?
- Q.2. What else should be included in the differential diagnosis?
- Q.3. What further investigations should be ordered?
- Q.4. What are the complications of this disease?
- Q.5. Name a few conditions which predispose to this disease.
- Q.6. Name a few oncogenes which are associated with this disease.

ANSWERS

- A.1.** In a middle-aged male with a history of weight loss, anaemia and change in bowel habit, along with troublesome piles, the most probable diagnosis is carcinoma of colon.
- A.2.** Carcinoma of colon should always be distinguished from colitis, diverticular disease, polyps, and ischaemic disease of the colon.
- A.3.**
- i. Faecal occult blood—At least four samples.
 - ii. Sigmoidoscopy and biopsy—colonoscopy
 - iii. Barium enema
 - iv. Carcinoembryonic antigen (CEA) for baseline levels.
- A.4.** These include:
- i. Perforation
 - ii. Localized and/or generalized peritonitis
 - iii. Severe rectal bleeding
 - iv. Obstruction—volvulus.
 - v. Pressure symptoms locally
 - vi. Fistulae
 - vii. Abscesses and abdominal wall cellulitis.
- A.5.** These include:
- i. Familial polyposis coli.
 - ii. Villous adenoma
 - iii. Adenomatous polyp.
 - iv. Ulcerative colitis.
- A.6.** The most commonly associated oncogenes with colonic cancer are c-KRAS and c-MYC which are expressed in up to 50 percent and 70 percent of tumours respectively. Other less frequently altered oncogenes include c-SRC and c-ERB-2.

29

C A S E

Peptic Ulcer

BRIEF HISTORY

A 60-year-old lady was taken to the doctor by her son with three-month history of general ill health, tiredness, swelling of legs and occasional confusion. The doctor found that she was pale and in mild heart failure and arranged for haemoglobin and other blood tests. Her haemoglobin was found to be 5.6 g/dl and she was admitted to the hospital for further investigations and treatment. She denied having abdominal pain but did admit to occasional indigestion and belching. There was no history of loss of appetite or weight, urinary or bowel symptoms. She was not a known diabetic or hypertensive and was taking no medications.

IMPORTANT CLUES ON CLINICAL EXAMINATION

On examination, she was anaemic and mildly confused. Blood pressure was 130/70 mmHg, pulse 88 per minute and regular and she had pitting oedema over both ankles. JVP was raised by two cm. There was no clubbing, cyanosis, thyroid enlargement or lymphadenopathy. Her liver was 3 cm. enlarged, soft, smooth and tender. There was no epigastric mass or tenderness and no splenomegaly or ascites. She had a few bilateral basal crackles. She was in sinus rhythm and had a soft systolic murmur at the apex without radiation. There were no localising neurological signs.

INVESTIGATIONS

Following were the results of various investigations:

Hb:	(repeated) 5.6 g/dl	Blood sugar:	6 mmol/l (108 mg/dl)
MCV:	72fl	Blood urea:	11 mmol/l (66 mg/dl)

Contd...

Contd...

WCC:	7.8 × 10 ⁹ /l	Creatinine:	98 umol/l (1.1 mg/dl)
	P:77% L:18%	Albumin:	3.0 g/dl
	M:3%E:2%	Faecal occult	
Platelets:	440 × 10 ⁹ /l	blood:	positive in 2 samples
ESR:	42 mm in 1st hour	Barium	
Sodium:	138 mmol/l	enema:	normal
Potassium:	3.6 mmol/l	ECG:	normal
Bicarbonate:	24 mmol/l	Chest X-ray:	heart size slightly
Chloride:	97 mmol/l		enlarged with pulmo- nary congestion

QUESTIONS

- Q.1. What is the likely diagnosis?
- Q.2. What two further investigations can help the diagnosis?
- Q.3. Give three complications of this disease.
- Q.4. How would you manage this patient?

ANSWERS

- A.1.** The most likely diagnosis in this lady with general ill health, indigestion, very low haemoglobin with low MCV, a normal barium enema with positive faecal occult blood is peptic ulcer. Peptic ulcer in old age may be completely asymptomatic or may present only with vague epigastric discomfort and "indigestion". This patient also has a mild heart failure, probably, as a result of severe anaemia.
- A.2.** i. Barium meal.
ii. Upper gastrointestinal endoscopy and biopsy.
- A.3.** i. Haemorrhage
ii. Perforation
iii. Obstruction.
- A.4.** i. Antacids.
ii. Antisecretory agents:
a. Pirenzepine (anti-muscarinic agent) 50 mg bd.
b. Proglumide (gastric receptor antagonist) 1.2 to 1.6 grams daily.
c. Cimetidine, ranitidine, famotidine, nizatidine, etc. (H_2 antagonists) 400 mg bd, 150 mg bd, 40 mg nocte and 150 mg respectively.
d) Omeprazole (proton pump $H^+K^+ATPase$ inhibitor) 20 mg daily or lansoprazole 30 mg daily. Others include pantoprazole, rabeprazole and esomeprazole.
iii. Cytoprotective agents: Misoprostil (prostaglandin inhibitor) 200 micrograms bd.

Other drugs include sucralfate, colloidal bismuth and carbenoxolone.

Recently, a lot of stress is on gastric biopsy and looking for *H. pylori* as this organism is directly associated with hyperacidity and ulceration. Once confirmed, histologically, patient can have different regimens one of which is omeprazole 20 mg bd, clarithromycin 500 mg bd and amoxycillin 1 g bd for ten days then continue with omeprazole for at least 28 days.

Other regimen is lansoprazole 30 mg od, clarithromycin 250 mg bd, and amoxycillin 1 gm bd for seven days.

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C A S E

Primary Biliary Cirrhosis

BRIEF HISTORY

A 56-year-old lady was referred to the medical outpatient clinic with an eight-month history of pruritus. She had loose motions for the last four weeks and felt generally tired. There was no history of loss of weight or appetite. She had been applying calamine lotion over her skin but with little relief though diarrhoea was a little better with kaopectate given by her doctor two days ago. She also had history of passing dark urine and pale stools and someone told her that her eyes had turned yellow as well. She was also worried about darkening of her skin.

IMPORTANT CLUES ON CLINICAL EXAMINATION

On examination, she was mildly icteric and had clubbing of her fingers. There was no lymphadenopathy or glandular enlargement. Blood pressure was 170/100 mmHg. Pulse rate was 80 per minute and regular. Her skin was a little dry and pigmented and she had scratch marks all over her body with bilateral xanthelasmae. Respiratory and cardiovascular systems were normal. Abdominal examination showed that liver was 6 cm enlarged, firm, smooth, and non-tender. The spleen was 3 cm enlarged and she had some shifting dullness but no definite fluid thrill could be elicited. Neurological examination was normal.

INVESTIGATIONS

Her initial investigations were as following:

Hb:	11g/dl	Blood sugar:	4.9 mmol/l (88 mg/dl)
	(normocytic	Blood urea:	3.5 mmol/l (21 mg/dl)
	normochromic)	Creatinine:	110 umol/l (1.2 mg/dl)

Contd...

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WCC:	$9 \times 10^9/l$	Total bilirubin:	26 $\mu\text{mol/l}$ (1.5 mg/dl)
	P:80% L:17%	Direct:	8 $\mu\text{mol/l}$ (0.5 mg/dl)
	M:2% E:1%	Indirect:	18 $\mu\text{mol/l}$ (1.0 mg/dl)
Platelets:	$290 \times 10^9/l$	Albumin:	3.8 g/dl
ESR:	55 mm in 1st hour	Alk. phos:	230 U/l
Sodium:	138 mmol/l	ECG:	normal
Potassium:	4.1 mmol/l	Chest X-ray:	normal
Bicarbonate:	24 mmol/l		
Chloride:	98 mmol/l		

QUESTIONS

- Q.1. What is the most likely diagnosis?
- Q.2. What four investigations will help the diagnosis?
- Q.3. How would you treat pruritus?
- Q.4. What other causes you know can result in similar disease?
- Q.5. What is Zieve's syndrome?

ANSWERS

- A.1.** The most likely diagnosis in this lady with prolonged pruritus, jaundice, hepatosplenomegaly and xanthelasmae is primary biliary cirrhosis, the cause is unknown.
- A.2.**
- i. Serum cholesterol level (high).
 - ii. Antimitochondrial antibodies. This is IgG and is present in 95 percent of cases.
 - iii. Serum IgM level (raised in 8% of cases).
 - iv. Liver biopsy (after correction of prothrombin time). This is characterized by destruction of medium and small bile ducts infiltration with acute and chronic inflammatory cells, fibroblastic reaction and bile stasis.
- A.3.** If the obstruction is incomplete, cholestyramine 8 to 12 gm daily in divided doses is helpful in controlling pruritus. Cholestyramine by binding bile acids in the gut increases their excretion. Antihistamines or topical lotions may be helpful. Rifampicin and naloxone hydrochloride (opioid antagonist) have been shown to be of benefit in trials.
- A.4.** Secondary biliary cirrhosis is characterised by obstruction of the large extrahepatic bile ducts which may be caused by impaction of gallstone or stricture formation.
- A.5.** Zieve's syndrome is characterised by alcoholic hepatitis, jaundice, haemolytic anaemia and hypercholesterolaemia. The condition is seen after a bout of heavy alcohol intake and, usually, settles if the person stops drinking.

Carcinoma Oesophagus

BRIEF HISTORY

A 66-year-old woman was admitted with an eighteen-month history of dyspepsia, heartburn and regurgitation made worse by lying flat at night and bending forwards. She had occasional difficulty in swallowing solid foods only. Her doctor diagnosed her as having hiatus hernia with reflux oesophagitis and she responded adequately with antacids and metochlopramide. For the last four weeks, her symptoms suddenly worsened and she started having increasing difficulty not only with solids but liquids as well with frequent vomiting containing small quantities of undigested food and a few streaks of blood. She had lost her appetite and was, in fact, scared of eating anything. She lost about 5 kg in weight over this period. She could sometimes feel the food sticking behind her sternum breast bone.

IMPORTANT CLUES ON CLINICAL EXAMINATION

On examination, she looked pale and emaciated. There was no thyroid or lymph node enlargement. Her throat appeared normal. Blood pressure was 140/80 mmHg, pulse was 84 per minute and regular. Skin was normal. There was no clubbing, cyanosis or jaundice. Abdominal examination was normal, in particular, there was no epigastric mass or tenderness. Rest of the systemic examination was normal, too.

INVESTIGATIONS

Following were the results of various investigations:

Hb:	8.9g/dl	Chloride:	96 mmol/l
	(hypochromic	Blood sugar:	8.4 mmol/l (151 mg/dl)
	microcytic)	Blood urea:	5.0 mmol/l (30 mg/dl)

Contd...

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WCC:	9.7 × 10 ⁹ /l	Creatinine:	100 µmol/l (1.1 mg/dl)
	P:77% L:20%	ECG:	normal except some
	M:2% E:1%		flattening of T waves
Platelets:	330 × 10 ⁹ /l		in left chest leads
ESR:	47 mm in 1st hour		(V3-V6)
Sodium:	138 mmol/l	Chest X-ray:	normal
Potassium:	4.0 mmol/l		
Bicarbonate:	25 mmol/l		

QUESTIONS

- Q.1.** What could be the diagnosis?
- Q.2.** Give a few other causes of dysphagia.
- Q.3.** Name a two most important investigations.
- Q.4.** What is Barrett's oesophagus?
- Q.5.** What treatments can be offered?

ANSWERS

- A.1.** This lady has already a long history of dyspepsia, heartburn and regurgitation which is characteristic of reflux oesophagitis and hiatus hernia. Her symptoms were only partially relieved with antacid and H₂-antagonists and had in fact, become more persistent during the last four weeks. Weight loss and worsening symptoms are certainly suggestive of carcinoma of lower end of the oesophagus.
- A.2.**
- i. Pseudobulbar palsy.
 - ii. Systemic sclerosis.
 - iii. Achalasia of the cardia.
 - iv. Oesophageal web (Plummer-Vinson/Patterson-Kelly syndrome).
 - v. Sjögren's syndrome.
- A.3.** Barium swallow—to see a stricture, probably malignant. Oesophagoscopy and biopsy is mandatory in these cases. The initial examination is not invariably adequate in differentiating cancer from benign inflammatory stricture, therefore, repeat endoscopy is important.
- A.4.** In this condition, there are islands of columnar gastric epithelium surrounded by squamous stratified epithelium of oesophagus. This predisposes to oesophageal carcinoma.
- A.5.**
- i. Palliative management by inserting a Celestin's tube or a feeding gastrostomy or PEG (per endoscopic gastrostomy).
 - ii. Surgical resection of the tumour if situated in the lower one-third of oesophagus with or without pre-operative radiotherapy and then anastomosis.
 - iii. Radiotherapy only for the cancers involving upper and middle third of oesophagus.

Chronic Hepatitis/Cirrhosis

BRIEF HISTORY

A 58-year-old woman was referred for further investigations by her doctor with moderate splenomegaly for no obvious cause. She admitted having excessive tiredness, lethargy and pain in her joints for the last four months, but she thought it was because she was getting old. She had been given a course of ampicillin six weeks ago for her cough and cold. She denied any history of serious illness in the past.

IMPORTANT CLUES ON CLINICAL EXAMINATION

On examination, she was not anaemic. There was no oedema, clubbing or lymphadenopathy. JVP was not raised. She was mildly jaundiced, but there were no spider naevi or palmar erythema. Her liver was 2 cm enlarged, smooth and non-tender. Spleen was 4 cm enlarged. There was no ascites. Respiratory, cardiovascular and central nervous systems were normal. She had oestho-arthritis of both knees but could walk unaided.

INVESTIGATIONS

The results of investigations were as follows:

Hb:	13 g/dl (normocytic normochromic)	Blood sugar:	9.8 mmol/l (176 mg/dl)
		Blood urea:	5.5 mmol/l (33 mg/dl)
		Creatinine:	89 µmol/l (1.0 mg/dl)
WCC:	$8 \times 10^9/l$	Bilirubin:	32 µmol/l (1.9 mg/dl)
	P:75% L:22%	AST:	190 U/l
	M:1% E:2%	Total proteins:	6.3 g/dl
Platelets:	$340 \times 10^9/l$	Albumin:	2.7 g/dl

Contd...

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ESR:	46 mm in 1st hour	Alk. Phos:	120 U/l
Sodium:	139 mmol/l	ECG:	normal
Potassium:	3.4 mmol/l	Chest X-ray:	normal
Bicarbonate:	26 mmol/l		
Chloride:	99 mmol/l		

QUESTIONS

- Q.1.** What is the differential diagnosis?
- Q.2.** What three further investigations will help to confirm your diagnosis?
- Q.3.** Name four more investigations that you consider are relevant.
- Q.4.** Name four conditions known to be associated with your final diagnosis.

ANSWERS

- A.1.** The differential diagnosis in this lady with ill health, hepatosplenomegaly, arthralgia, raised serum enzymes and bilirubin, low serum albumin and high globulin is chronic hepatitis or cirrhosis of liver. Others include lymphoma or auto-immune disorders.
- A.2.**
- i. Liver biopsy lymphocytic or plasma cell infiltration.
 - ii. Serum immunoglobulin assay: (IgG in excess of 2 gm percent).
 - iii. Persistent elevation of hepatic enzymes.
- A.3.**
- i. HBsAg and anti-HCV antibodies.
 - ii. Alpha fetoprotein.
 - iii. Autoantibodies, e.g., antinuclear, smooth muscle and antimitochondrial antibodies.
 - iv. Lymph node biopsy if palpable and accessible.
- A.4.**
- i. Ulcerative colitis.
 - ii. Hashimoto's disease
 - iii. Thyrotoxicosis
 - iv. Glomerulonephritis.

Meningitis

BRIEF HISTORY

A 23-year-old office clerk was admitted with a two-day history of sore throat and headaches. On the day of admission, he woke up with high grade fever, felt chills and had painful joints. His wife told that he also had vomitted whatever he ate and was a bit confused and irritable which was not right for his usual self. He had enjoyed good health, but felt that he had been under undue pressure in his job during the recent month. Four years ago, he made an uneventful recovery from a very bad sore throat which was diagnosed as glandular fever. There were no other illnesses in the past. He smoked 20 cigarettes a day. He was not taking any medications except for headaches off and on.

IMPORTANT CLUES ON CLINICAL EXAMINATION

On examination, he was a bit restless and agitated. His temperature was 101°F. Blood pressure was 120/70 mmHg. Pulse was 98 per minute and regular. There was no anaemia, cyanosis, jaundice or oedema. Thyroid and lymph nodes were not enlarged. He had petechial rashses on his soft palate, both axillae and flanks. The rash on the flanks was irregular macular rash and extended to buttocks. His throat was congested. His abdomen was soft. Liver was not enlarged, but the spleen tip was palpable. He had neck rigidity and photophobia, but the examinations of fundi, cranial nerves, motor-sensory system and reflexes were normal.

INVESTIGATIONS

Following were the results of the initial investigations:

Hb:	11 g/dl (normocytic normochromic)	Blood sugar: 6.6 mmol/l (119 mg/dl) Blood urea: 5.5 mmol/l (33 mg/dl) Creatinine: 108 umol/l (1.2 mg/dl)
WCC:	14.4 × 10 ⁹ /l P:81% L:17% M:2% E:0%	Urine: protein traces, 1-2pus cells/hpf, no RBC's ECG: found
Platelets:	250 × 10 ⁹ /l	sinus tachycardia, no
ESR:	14 mm in 1st hour	Chest X-ray: ischaemia or infarction
Sodium:	135 mmol/l	heart size normal, no
Potassium:	4.7 mmol/l	evidence of active lung
Bicarbonate:	20 mmol/l	lesion seen.
Chloride:	98 mmol/l	
Paul Bunnell test:	negative	

QUESTIONS

- Q.1.** What is your most likely diagnosis?
- Q.2.** What four further investigations will you ask for?
- Q.3.** Name three serious complications of this diagnosis.
- Q.4.** Name three antibiotics of choice for treating this condition.
- Q.5.** Discuss prophylaxis against this disease.
- Q.6.** Describe the rash which occurs in septicaemia due to this causative organism.

ANSWERS

- A.1.** The most likely diagnosis in this young patient with sore throat, headaches, pyrexia, petechial rashes in axillae, flanks and palate, pharyngitis, photophobia, neck stiffness, no lymphadenopathy raised, white cell count with polymorph leucocytosis, normal platelet count and negative Paul-Bunnell test is meningitis and most probably it is bacterial (*Meningococcal*) meningitis.
- A.2.**
- Lumbar puncture—for Gram staining, ZN stain for AAFB, protein and sugar content.
 - Blood cultures
 - Urine culture and sensitivity.
 - Throat swab culture.
- A.3.**
- Meningococcal septicaemia.
 - Disseminated intravascular coagulation (DIC).
 - Acute adrenal haemorrhage (Waterhouse-Friderichsen syndrome), which is essentially a post-mortem diagnosis.
- A.4.**
- Benzyl Penicillin: 12 to 24 megaunits (millions) per 24 hours IV, and then rifampicin 450 mg bid for two days at the end of therapy.
 - Cefotaxime: 2 grams six hourly IV.
 - Chloramphenicol: 1 gram six hourly IV.
- A.5.** There has been development of high molecular weight polysaccharides antigen from organisms of serogroup A and C. For prophylaxis of intimate relatives, rifampicin 600 mg daily for 4 days or minocycline in dosage of 100 mg every 12 hourly for 5 days.
- A.6.** The rash is petechial and occurs in axillae, legs, thighs, buttocks and feet and this becomes confluent and is called “Purkinje rash”. Aspirates from the rash may reveal Gram-negative diplococci.
- NB:** Currently, ceftriaxone, a third generation cephalosporin is used in a dose of 2 Gm IV 12 hourly for 5 to 7 days.

Parkinsonism

BRIEF HISTORY

A man of 62 was admitted with a history of frequent falls and poor mobility for the last six months. His son had noticed that his father was quiet most of the time and had staring look with glazed eyes. He also noticed that while walking, he used to shuffle a little bit and could not turn around quickly. There was no history of associated convulsions or loss of consciousness. He was not incontinent of urine or faeces and there was no loss of memory either.

IMPORTANT CLUES ON CLINICAL EXAMINATION

On examination, he was found to be mentally alert, his blood pressure was 170/100 mmHg, pulse was seventy-six per minute and regular. JVP was normal and there was no oedema, lymphadenopathy or carotid bruit. He had rather a staring look with infrequent blinking and poor expression on his face and had a soft and low voice. His chest and cardiovascular systems were normal. He was noted to have some tremour of his right thumb and fingers at rest. The tone was somewhat increased in all his limbs, but the reflexes were normal.

INVESTIGATIONS

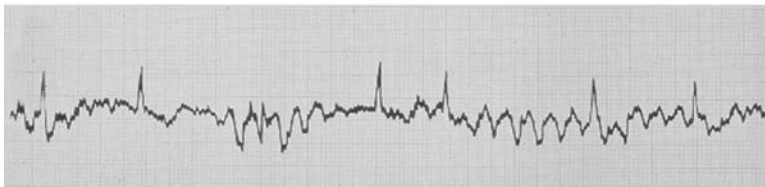
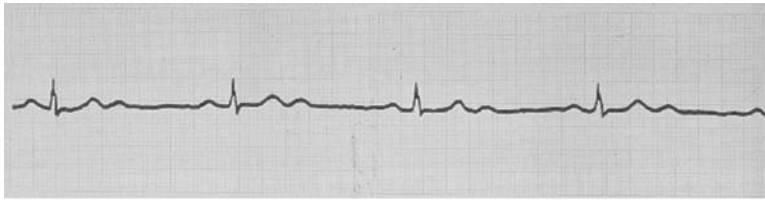
Following were the results of various investigations:

Hb:	13.1 g/dl (normocytic normochromic)	Chloride:	101 mmol/l
		Blood sugar:	7.5 mmol/l (135 mg/dl)
		Blood urea:	10.3 mmol/l (62 mg/dl)
WCC:	$9.2 \times 10^9/l$	Creatinine:	128 μ mol/l (1.2 mg/dl)
	P:76% L:20% M:2% E:2%	ECG:	as shown in the Figure 34.1
		Chest X-ray:	normal heart size,

Contd...

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Platelets:	280 × 10 ⁹ /l	no lung lesion seen.
ESR:	28 mm in 1st hour	
Sodium:	144 mmol/l	
Potassium:	4 mmol/l	
Bicarbonate:	23 mmol/l	



(b)

Fig. 34.1: (a) Hypokalaemia (Note U wave) and (b) Parkinsonism

QUESTIONS

- Q.1. What is the most likely diagnosis?
- Q.2. What is the differential diagnosis?
- Q.3. What is the most widely used drug for this condition?
- Q.4. What are the common side effects of this drug?
- Q.5. What are the new drug regimens of this disorder?
- Q.6. Why the patients with this disease fall down while turning around?
- Q.7. What are Steele-Richardson-Olszewski syndrome and Shy-Drager syndrome?

ANSWERS

- A.1.** Clinical manifestations, such as tremour at rest, rigidity and poverty of movements, expressionless face and soft low voice, all favour a diagnosis of parkinsonism. The diagnosis is not always easy, especially in the early stages when the clinical features may not be marked and this can easily be confused with depression.
- A.2.** i. Drugs like phenothiazine derivatives.
ii. Postencephalitic parkinsonism(encephalitis lethargica).
iii. Arteriosclerotic parkinsonism.
- A.3.** Levodopa—which is marketed under two brand names:
— Sinemet (Levodopa and carbidopa)
— Madopar (Levodopa and benzserazide)
- A.4.** i. Nausea and vomiting.
ii. Confusion, depression, and hallucinations.
iii. Worsening of tremours.
iv. Postural hypotension.
- A.5.** Selegilene (Eldepryl) which is a mono-amine oxidase type B inhibitor is quite good in controlling symptoms of parkinsonism. It basically increases the concentration of dopamine in the brain by preventing its breakdown by mono-amine oxidase type B.
Pergolide (Celance) which is dopamine agonist.
Tolcapone (Tasmar) which is a catechol-O-methyl transferase (COMT) inhibitor. Entacapone (Comtess) has no hepatotoxicity as compared to Tolcapone which has been withdrawn from the market.
- A.6.** These patients are rigid and bradykinesic, therefore, when they suddenly turn around, their body moves, but the movement at ankles is not coordinated, therefore, they fall. But if they are asked to turn around slowly and in short steps, this can be easily prevented.
- A.7.** The former is characterised by progressive paralysis of voluntary vertical eye movements, dysarthria and axial rigidity with onset in middle or later life.
The latter is characterised by autonomic failure with severe postural hypotension and often akinesia and rigidity.

BRIEF HISTORY

A man of 36 was admitted via casualty to the acute medical unit with coma. History from the wife suggested that he had been generally unwell for the last fortnight and had been forgetful at times and was also getting progressively short of breath on exertion. He had also complained of occasional headaches. The wife had noted that her husband was getting swelling of both his legs for the last two months. He had been frequently taking aspirin tablets for his headaches but preferred not to bother about his health.

Further history from the wife revealed that the patient had retired to bed about ten o'clock in the evening and after an hour was found to be fitting by his wife and then he became unconscious.

IMPORTANT CLUES ON CLINICAL EXAMINATION

On examination, he was unarousable and did not respond to painful stimuli. His blood pressure was 240/140 mmHg which was checked twice, pulse was 80 per minute and regular. JVP was raised by four centimetres and there was pitting oedema of both his legs. There was no neck stiffness. The right pupil was widely dilated and sluggish to react with light. The fundi showed papilloedema, arteriovenous nipping, flame shaped haemorrhages and soft exudates on both sides. There was grade III weakness of his left lower limb and left plantar was upgoing with generalised hyper-reflexia. Apex beat was in the sixth intercostal space, two centimetres outside the mid-clavicular line and there was a pansystolic murmur over the apex radiating to the left axilla. Lung bases were full of crepitations, but the air entry was not impaired.

INVESTIGATIONS

Results of various investigations were as follows:

Hb:	12.4 g/dl (normocytic normochromic)	Blood sugar: 10 mmol/l (180 mg/dl) Blood urea: 8 mmol/l (48 mg/dl) Creatinine: 138 μ mol/l (1.5 mg/dl)
WCC:	8×10^9 /l P:72% L:26% M:1% E:1%	Urine: normal ECG: left axis deviation with marked left ventricular hypertrophy and strain.
Platelets:	310×10^9 /l	Chest X-ray: cardiomegaly with moderate pulmonary congestion.
ESR:	13 mm in 1st hour	
Sodium:	142 mmol/l	
Potassium:	4.2 mmol/l	
Bicarbonate:	28 mmol/l	
Chloride:	99 mmol/l	

QUESTIONS

- Q.1.** What is the most likely diagnosis, and why?
- Q.2.** What is the classical vascular lesion in this condition?
- Q.3.** What are three important aspects of his immediate therapy?
- Q.4.** List a few conditions associated with your final diagnosis.
- Q.5.** What are the factors which indicate an adverse prognosis in this condition?

ANSWERS

- A.1.** Accelerated hypertension (high blood pressure with papilloedema) with sign of stroke and a grand mal fit all point towards a diagnosis of hypertensive encephalopathy in this patient. The patient had a massive right sided intracerebral bleed. Subarachnoid haemorrhage is another possibility, but the absence of neck stiffness and subhyaloid haemorrhages make it less likely, though in deeply comatosed patient neck rigidity is absent. Cerebral haemorrhage is usually associated with more marked focal neurological signs.
- A.2.** The characteristic vascular lesion is fibrinoid necrosis of the walls of small arteries and arterioles and this can be reversed by effective anti-hypertensive agents.
- A.3.**
- i. Gently control his blood pressure by isoket infusion. Other agents are sodium nitroprusside and methyl-dopa.
 - ii. Treat the heart failure by parenteral loop diuretics such as frusemide.
 - iii. Use dexamethasone to reduce the cerebral oedema.
- A.4.**
- i. Pheochromocytoma.
 - ii. Gout.
 - iii. Acromegaly.
 - iv. Cohn's syndrome (primary hyperaldosteronism).
 - v. Cushing's syndrome.
- A.5.**
- i. Black race
 - ii. Young age
 - iii. Male
 - iv. Diastolic pressure persistently above 115 mmHg
 - v. Diabetes mellitus
 - vi. Obesity
 - vii. Smoking
 - viii. Evidence of damage of end organs such as heart, eyes, kidneys, brain and eyes.

Shy-Drager Syndrome

BRIEF HISTORY

A 72-year-old male presented to the out-patient department with a history of slowing of movements and recurrent falls. He was known to have Parkinson's disease for the last seven years but was well controlled with medications which included levodopa and anticholinergics. There was history of occasional sweating. He was reluctant to move and was mostly bed bound. Nothing else significant was present in the past history.

IMPORTANT CLUES ON CLINICAL EXAMINATION

On examination, he had a mask like face and monotonous voice. His face was shiny and blinking was decreased. Pulse was 80 per minute and regular. His blood pressure was 120/85 mmHg while sitting and 100/70 mmHg on standing. Cardiovascular, respiratory and abdominal examinations were normal. Neurologically, he had cog wheel type rigidity and a positive glabella type.

INVESTIGATIONS

Following investigations were carried out:

Hb:	13.2 g/dl (normocytic normochromic)	Bicarbonate:	24 mmol/l
		Chloride:	102 mmol/l
WCC:	$9.2 \times 10^9/l$ P:76% L:20% M:2% E:2%	Blood urea:	5 mmol/l (30 mg/dl)
		Creatinine:	112 μ mol/l (1.3 mg/dl)
Platelets:	$280 \times 10^9/l$	Blood sugar:	6 mmol/l (108 mg/dl)
ESR:	15 mm in 1st hour	Urine:	normal
Sodium:	140 mmol/l	ECG:	no ischaemic changes
Potassium:	4.4 mmol/l	Chest X-ray:	normal

QUESTIONS

- Q.1.** What is the most likely diagnosis?
- Q.2.** What is the differential diagnosis?
- Q.3.** How would you manage such cases?

ANSWERS

- A.1.** In a patient who is known to have Parkinson's disease for years and is on treatment, develops significant postural drop in blood pressure resulting in falls favours a diagnosis of Shy-Drager syndrome, which is a rarity and is due to involvement of autonomic nervous system.
- A.2.** The differential diagnosis includes all the causes leading to postural hypotension and falls. Levodopa therapy itself causes hypotension. Other drugs, e.g. thiazide diuretics, tricyclic agents, phenothiazines and benzodiazepines may cause hypotension. Prolonged bed rest also leads to orthostatic hypotension. Vertebrobasilar insufficiency can also lead to hypotension by stimulating autonomic plexus around the blood vessels carrying blood to the brain.
- A.3.** Management begins with reduction or discontinuation of the causative drug, e.g. levodopa.

Raising the head end of the bed at night may be helpful.

Treatment with fludrocortisone 0.1 mg (100 ug) to 0.3 mg (300 ug) per day may be helpful.

Tight full length elastic stocking and advice on the gradual achievements of the standing position from lying.

NB: In 1960, Shy and Drager drew attention to a syndrome characterized by autonomic failure with severe postural hypotension and often akinesia and rigidity. These patients show loss of pre-ganglionic sympathetic neurons. In addition, there often is severe cell loss and gliosis in the olivopontocerebellar and striatonigral regions.

Brain Tumour

BRIEF HISTORY

A 38-year-old male presented to the medical outpatient department with a history of episodic left-sided headache. The headache was moderate to severe in intensity and it had no relationship with food or exertion. He did mention that for the last two weeks, the headache was quite severe in the morning and it made him vomit as well. He was accompanied by his wife who told that for the last one week, he was becoming forgetful and had irrational behaviour with his friends, relatives and even with her. He also had become more lethargic and drowsy and had complained of giddiness. Three days ago, he had generalized convulsions. In the past, he had no serious illnesses and there was no history of head injury, diabetes or hypertension.

IMPORTANT CLUES ON CLINICAL EXAMINATION

On examination, he was well built. General physical examination was normal. Pulse was 64 per minute and regular, and his BP was 140/95 mmHg. Respiratory, cardiovascular and abdominal examinations were normal. His speech was normal. Orientation was mildly disturbed. Cranial nerves were intact. There was weakness in the right half of the body of grade iv but no sensory impairment. On fundoscopy, there was evidence of papilloedema on left side. There was no neck stiffness and Kernig's sign was absent.

INVESTIGATIONS

Following investigations were available:

Hb:	14.5 g/dl (normocytic normochromic)	Bicarbonate: 24 mmol/l Chloride: 102 mmol/l
WCC:	$8.4 \times 10^9/l$ P:76% L:21% M:2% E:1%	Blood urea: 6 mmol/l (36 mg/dl) Blood sugar: 6.6 mmol/l (119 mg/dl) Creatinine: 126 μ mol/l (1.4 mg/dl)
Platelets:	$320 \times 10^9/l$	Urine: normal
ESR:	14 mm in 1st hour	ECG: normal
Sodium:	136 mmol/l	X-ray skull: no obvious abnormalities
Potassium:	3.4 mmol/l	

QUESTIONS

- Q.1.** What is the most likely diagnosis?
- Q.2.** What are three confirmatory diagnostic tests?
- Q.3.** What is the significance of a chest X-ray?
- Q.4.** What is the differential diagnosis?
- Q.5.** Name lesions which tend to produce more or less similar symptoms without prominent localising signs.
- Q.6.** Discuss the prognosis.

ANSWERS

- A.1.** In a patient with a history of headaches, right-sided weakness, change in personality and a seizure, the most likely diagnosis is a brain tumour.
- A.2.** These include:
- i. CT scan—investigation of choice.
 - ii. MRI—particularly for posterior fossa tumour.
 - iii. EEG—may show electrical abnormalities.
- A.3.** Chest X-ray is an important investigation and should be done routinely to rule out any primary tumour (bronchogenic carcinoma) and brain metastases from that.
- A.4.** General symptoms of a space occupying lesion (S.O.L) should be differentiated from:
- i. Pseudotumour cerebri.
 - ii. Hypertensive encephalopathy.
 - iii. Chronic obstructive airway disease due to hypercapnoea.
 - iv. Thrombosis of cerebral veins.
 - v. Tuberculous meningitis.
 - vi. Addison's disease and hypoparathyroidism.
 - vii. Severe vitamin A deficiency.
 - viii. Hydrocephalus.
- A.5.** These include:
- i. Medulloblastoma.
 - ii. Ependymoma.
 - iii. Haemangioblastoma of cerebellum.
 - iv. Pinealoma.
 - v. Colloid cyst of the third ventricle.
 - vi. Craniopharyngioma.
- A.6.** It is influenced by the nature of the growth, its location and other factors. Almost all intracranial tumours are fatal if operation is not performed. Most fatal tumours are glioblastomas. Astrocytomas grow slowly and permit survival for many years. One should also not forget the perioperative and postoperative mortality. Long-term corticosteroid therapy may be required for raised intracranial pressure when the tumour is inoperable. With all malignant brain tumours, the overall outlook is poor with less than 50 percent survival at one year. Meningiomas, when removed in total, are curable.

Viral Encephalitis

BRIEF HISTORY

A 16-year-old boy was admitted via accident and emergency department with a four-hour history of generalized fits. Two days prior to his admission, he complained of flue-like illness and was prescribed paracetamol. He kept on attending his school but complained of vague headaches and fever which was of high grade. One day before admission, he became unduly irritable and parents told that his behaviour was a bit odd. There was no history of such illness in the family. The fit was generalized and patient had incontinence of urine, and also bit his tongue.

IMPORTANT CLUES ON CLINICAL EXAMINATION

On examination, he was comatosed and both pupils were dilated. His temperature was 103°F and there was no cyanosis clubbing or lymphadenopathy. BP was 110/70 mmHg. Pulse was 68 per minute and regular. Heart sounds were normal. Chest was clear. Abdominal examination was unremarkable. He was deeply comatosed and both eyes were diverged. He had neck stiffness, hyper-reflexia and upgoing plantars. On fundoscopy, the right optic disc was blurred, while there was papilloedema on the left side.

INVESTIGATIONS

Following investigations were carried out:

Hb:	14.4 g/dl	Chloride:	100 mmol/l
	(normocytic	Blood urea:	8 mmol/l (48 mg/dl)
	normochromic)	Blood sugar:	6 mmol/l (108 mg/dl)

Contd...

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WCC:	12.4 × 10 ⁹ /l	Creatinine:	105 umol/l (1.2 mg/dl)
	P:78% L:18%	Urine:	normal
	M:3% E:1%	ECG:	sinus bradycardia, nil
Platelets:	350 × 10 ⁹ /l		else of note
ESR:	16 mm in 1st hour	Chest X-ray:	normal.
Sodium:	140 mmol/l		
Potassium:	4.2 mmol/l		
Bicarbonate:	25 mmol/l		

QUESTIONS

- Q.1.** What is the likely diagnosis?
- Q.2.** What is the single most important differential diagnosis?
- Q.3.** What further investigations would you ask for?
- Q.4.** What is the significance of titres against the organism causing this disease?
- Q.5.** What is the classical histological hallmark of this disease?

ANSWERS

- A.1.** In a young boy with a history of fever, flue-like illness and sudden deterioration in consciousness with previous irritability and then a grand mal fit with papilloedema indicates a rapidly occurring intracerebral pathology, most probably a viral encephalitis.
- A.2.** Acute bacterial meningitis should be an important diagnosis to rule out, but there are no personality changes in bacterial meningitis and the downhill course is not so rapid. Other diagnoses should include cerebral abscess, disseminated encephalomyelitis and toxic confusional state in febrile illness and septicaemia.
- A.3.**
- i. *Electroencephalogram (EEG)*: This is diffusely abnormal. Slow delta waves bilaterally, are of high amplitude and tend to be more conspicuous over the frontal region.
 - ii. *CT scan*: It is safer and can show diffuse cerebral oedema before one plans lumbar puncture.
 - iii. *Lumbar puncture*: This should not be done in every case and it is better to document any raised intracranial pressure. The CSF fluid samples are completely normal or contain a few to several hundred white cells which are mononuclear or polymorphonuclear. If the CSF is grossly blood stained, it is a grave sign.
- A.4.** The rise in titres does not determine the diagnosis of encephalitis because rises do occur non-specifically with bacterial pneumonia or bacterial meningitis and uncomplicated *herpes labialis* and other conditions.
- A.5.** This is cowdry type A ("Owl-Eye") intranuclear inclusions in the brain cells.
- N.B:** Suspected *herpes simplex encephalitis* is immediately treated with intravenous acyclovir (10 mg/kg 8 hourly) the active form of which inhibits DNA synthesis. Phosphorylation of this drug is dependent upon the presence of viral thymidine kinase, thus, the drug is specific for herpes virus infections. The treatment should be continued for at least 10 to 14 days.

Motor Neuron Disease

BRIEF HISTORY

A 49-year-old mechanic attended the medical outpatient department with a six-month history of progressively increasing weakness of his arms and legs and difficulty in walking. He also noticed that he could not even stand up without help, and therefore, had started using a walking stick for the last two months, but during the last two months he had developed problems with feeding and choked on swallowing food which occasionally regurgitated through his nose. The wife noticed that his speech was also nasal. He did not complain of diplopia, though he had twitching of a few muscles.

IMPORTANT CLUES ON CLINICAL EXAMINATION

On examination, he was mentally alert. Blood pressure was 160/80 mmHg and pulse was 80 per minute and regular. Thyroid and lymph nodes were not enlarged and there was no clubbing or anaemia. Peripheral pulses were palpable. Examinations of cardiovascular, respiratory system and abdomen were normal. All cranial nerves were intact. There was marked bilateral wasting and weakness of shoulder girdle muscles with winging of the scapulae. He had claw hand deformity on the left side. There was marked fasciculation over both upper arms and thighs. There was some wasting and weakness of muscles of both lower limbs. Tendon reflexes were depressed in the upper limbs but brisk in lower limbs with upgoing plantars. There was no sensory impairment.

INVESTIGATIONS

Initial investigations were as follows:

Hb:	14.2 g/dl (normocytic normochromic)	Bicarbonate:	4.5 mmol/l
		Chloride:	102 mmol/l
WCC:	$9 \times 10^9/l$ P:74% L:22% M:3% E:1%	Blood urea:	5 mmol/l (30 mg/dl)
		Creatinine:	84 μ mol/l (0.9 mg/dl)
		Blood sugar:	9 mmol/l (162 mg/dl)
Platelets:	$270 \times 10^9/l$	Urine:	normal
ESR:	10 mm in 1st hour	ECG:	normal
Sodium:	139 mmol/l	Chest X-ray:	normal
Potassium:	4.1 mmol/l		

QUESTIONS

- Q.1. What is the most likely diagnosis?
- Q.2. What four investigations will you ask for?
- Q.3. What is the prognosis of this condition?
- Q.4. What are the sub-types of this disease?
- Q.5. What is the difference between fasciculations and fibrillations?
- Q.6. What drug may help in treating this disease?

ANSWERS

- A.1.** The most likely diagnosis in this man with gradually increasing weakness and wasting of his arms and legs with fasciculations with no diplopia, no sensory loss and intact sphincters is motor neurone disease (MND).
- A.2.** i. Electromyography (EMG).
ii. Nerve conduction studies (NCS).
iii. Muscle biopsy.
iv. Serum creatine phosphokinase levels.
- A.3.** Unfortunately, the prognosis in most cases is poor with death due to respiratory failure and bronchopneumonia within 2-3 years after the onset of symptoms.
- A.4.** There are four types:
i. Bulbar type.
ii. Pseudobulbar type.
iii. Amyotrophic lateral sclerosis.
iv. Progressive muscular atrophy.
- A.5.** The former is visible and is due to contraction of group of myofibrils while the latter is invisible and is due to contraction of individual myofibril and is an electromyographic phenomenon.
- A.6.** Riluzole (Rilutek) is the drug which is a glutamate antagonist. Glutamic acid in excess, damages the cells of motor neurons. Riluzole, in this way, slows down the process after six months to one year therapy, but it is very expensive.

Moyamoya Disease

BRIEF HISTORY

A 31-year-old male was admitted after an episode of convulsions lasting for ten minutes, involving the right side of his body including the face. During this episode he remained conscious and there was no tongue biting or incontinence of urine or faeces. For the past six months he had intermittent frontal headaches. There was no history of hypertension or diabetes. No allergies were noticed.

IMPORTANT CLUES ON CLINICAL EXAMINATION

On examination, he was conscious. Pulse was 80 per minute and regular. BP was 130/90 mmHg. Cardiovascular, respiratory and abdominal examinations were unremarkable. He was, however, aphasic and both eyes were deviated towards left. He had right facial nerve palsy of upper motor neurone type and no other cranial nerves were involved. Power in the right upper limb was of grade zero while it ranged from grade II to grade III in the right lower limb. Tendon reflexes were exaggerated on the right side and right plantar was extensor. Fundoscopy did not reveal any haemorrhages or papilloedema.

INVESTIGATIONS

Following investigations were carried out:

Hb:	14.2 g/dl (normocytic normochromic)	Chloride:	99 mmol/l
		Blood sugar:	5.2 mmol/l (94 mg/dl)
		Blood urea:	5.2 mmol/l (31 mg/l)
WCC:	$8.9 \times 10^9/l$ P 74% L 20% M 4% E 2%	Creatinine:	90 μ mol/l (1.0 mg/dl)
		Urine:	normal
		Chest X-ray:	within normal limits

Contd...

Contd...

Platelets:	$360 \times 10^9/l$	Auto anti-
ESR:	10 mm in 1st hour	body screen: negative
Sodium:	140 mmol/l	Syphilis
		serology: negative
Potassium:	4.2 mmol/l	ECG: normal
Bicarbonate:	24 mmol/l	

QUESTIONS

- Q.1. Name four more investigations.
- Q.2. What may be the most likely diagnosis?
- Q.3. What is the name given to the disease with malformed cerebral blood vessels?
- Q.4. What treatment can be offered?

ANSWERS

A.1. These include:

- i. Electroencephalogram (EEG): May show marked left central hemisphere abnormality.
- ii. Radioisotope brain scan: Increased activity in the left side of brain.
- iii. CT scan brain: May show a haematoma or a space occupying lesion on the left side of brain.
- iv. Carotid angiography: May show an arterio-venous malformation, aneurysm or other vascular pathology.

A.2. In a young male with sudden onset of convulsions and leading to paralysis of one side of the body, one should suspect a cerebrovascular catastrophe, a rupture of an aneurysm or a blood vessel situated in the substance of the cerebral hemisphere or congenitally malformed blood vessel. This later condition is diagnosed only on carotid angiography and is called moyamoya disease (MMD).

A.3. This is a congenital malformation of the internal carotid artery causing occlusion distal to the clinoid process and characterized by extensive collateral network. Moyamoya is a Japanese word meaning "Puff of Smoke". The aetiology remains obscure, however, at autopsy, fibrous thickening of the tunica intima of the internal carotid artery with degeneration of the tunica elastica and fibrosis of tunica media has been reported. It is more common in the Japanese.

A.4. The treatment is primarily symptomatic and supportive. Procedures, such as peri-vascular sympathectomy of the cervical part of carotid artery, superior cervical ganglion sympathectomy, arterial anastomosis and intracranial transplantation of omentum, have been tried but their effectiveness is not proven. Prognosis is variable and depends on the severity of the clinical picture.

Acoustic Neuroma

BRIEF HISTORY

A 52-year-old male presented to the outpatient department with a history of increasing headaches and noises in the right ear for the last one year. He also complained of difficulty in hearing and on two occasions had giddy turns in the past. The headaches were mostly in the morning and radiated from back of the head to the front and once it was followed by vomiting. He was a smoker but not a known hypertensive or diabetic. There was no family history of such complaints.

IMPORTANT CLUES ON CLINICAL EXAMINATION

On examination, he was in distress and had a band tied around his head. General physical examination was normal. Pulse was 62 per minute and regular and BP was 145/92 mmHg. Cardiovascular, respiratory and abdominal examinations did not reveal any abnormality. Higher mental functions were intact. Hearing on the right side was reduced. There was also facial weakness on the right side. The corneal reflex was absent and there was sensory impairment to touch, pain and temperature in the distribution of the trigeminal nerve on the right side. Lateral rectus on the right side was also weak. Nystagmus was also present on the right side with a fast component away from this side. There were no signs of meningeal irritation and other findings of motor and sensory systems were normal.

INVESTIGATIONS

Routine investigations showed:

Hb:	15.6 g/dl (normocytic normochromic)	Chloride	99 mmol/l
		Blood sugar:	4.0 mmol/l (72 mg/dl)
WCC:	$8.2 \times 10^9/l$ P 78% L 16% M 5% E 1%	Blood urea	5.2 mmol/l (31 mg/l)
		Creatinine	110 mg/dl (1.2 mg/dl)
Platelets:	$220 \times 10^9/l$	Urine:	normal
ESR:	20 mm in 1st hour	Chest X-ray:	within normal limits
Sodium:	140 mmol/l	ECG:	some ischaemia in lateral chest leads
Potassium:	4.5 mmol/l		
Bicarbonate:	25 mmol/l		

QUESTIONS

- Q.1.** What is the diagnosis?
- Q.2.** What further investigations are required?
- Q.3.** Name any association of this disease.
- Q.4.** What is the treatment?

ANSWERS

- A.1.** In a patient with a history of progressive deafness, dizziness, headaches and clinical findings of trigeminal, facial and abducens nerve involvement on the right side along with nystagmus point towards a lesion in the right cerebellopontine area—most probably an acoustic neuroma.
- A.2.** These include:
- i. X-ray of the skull: It will show erosion of the petrous part of the temporal bone on the internal acoustic meatus by the tumour.
 - ii. CT scan: This will outline the tumour and shows its extent. They are usually lucent to isodense, enhance greatly with contrast and are not calcified.
 - iii. MRI helps further defining the extent of the tumour.
- A.3.** This is associated with neurofibromatosis or von Recklinghausen's disease.
- A.4.** This depends on the extent of the tumour. Early detection can be useful for excision of the tumour.
Local radiotherapy is another mode of treatment.

Multiple Sclerosis

BRIEF HISTORY

A 28-year-old female presented to the medical outpatient department with pain in the eye and blurring of vision for the last three months which was episodic in nature. She also complained of dizzy spells which were accompanied by feeling of clumsiness in her left arm and left leg which she described as heavier than the right, but this lasted only for about a week or so. She also mentioned about feelings of numbness in the feet for the last four days. There was no such history in the family. She was married and had two children, both well.

IMPORTANT CLUES ON CLINICAL EXAMINATION

On examination, she was of good built and general physical examination was normal. Pulse was 80 per minute and regular and BP was 120/80 mm Hg. Cardiovascular, respiratory and abdominal examinations were unremarkable. Her mental functions were intact and there were no cranial nerve involvement except that she had mild pallor of the temporal sides of both optic discs on fundoscopic examination. Nystagmus was present. Her gait was little spastic. Power in upper limbs was normal while grade IV in the lower limbs with brisk reflexes and extensor plantars. There were no signs of meningeal irritation.

INVESTIGATIONS

Investigations revealed:

Hb:	13.2 g/dl	Bicarbonate:	25 mmol/l
	(normocytic	Chloride:	99 mmol/l
	normochromic)	Blood glucose:	4.6 mmol/l (83 mg/dl)

Contd...

Contd...

WBC:	9.2 × 10 ⁹ /l	Blood urea:	5.2 mmol/l (32 mg/l)
	P 75%, L 20%,	Creatinine:	82 umol/l (0.9 mg/dl)
	M 3% E 2%		
Platelets:	320 × 10 ⁹ /l	Urine:	normal
ESR:	20 mm in 1st hour	Chest X-ray:	normal
Sodium:	140 mmol/l		
Potassium:	3.9 mmol/l		

QUESTIONS

- Q.1. What is the possible diagnosis?
- Q.2. What is the differential diagnosis?
- Q.3. What further investigations are required to confirm diagnosis?
- Q.4. What is Lhermitte's sign and Uthoff's phenomenon?
- Q.5. What are other diseases of same category?
- Q.6. What treatment modalities are available?

ANSWERS

- A.1.** In a young female with relapsing symptoms of paraesthesia, retrobulbar pain, diplopia, nystagmus, hyper-reflexia and extensor plantars, the probable diagnosis is multiple sclerosis also called disseminated sclerosis.
- A.2.** In a classical case, the diagnosis is quite clear, but it has to be differentiated from following conditions:
- i. Behcet's disease
 - ii. Neurological sarcoidosis
 - iii. Meningovascular syphilis
 - iv. Cervical myelopathy
 - v. Subacute combined degeneration of cord
 - vi. Brainstem glioma
 - vii. Compression of optic chiasma.
- A.3.** These include:
- i. Cerebrospinal fluid (CSF) examination for:
 - a. Lymphocytosis (seldom above $0.05 \times 10^9/l$)
 - b. Raised total proteins (not above 1.2 g/l)
 - c. Paretic type of Lange's colloidal gold curve
 - d. Raised IgG levels
 - e. Oligoclonal gammaglobulin bands
 - ii. Visual evoked potentials:- Abnormal potentials are recorded in patients with multiple sclerosis
 - iii. CT scan may be of some help to show low density areas in the white matter of cerebral hemisphere
 - iv. Magnetic resonance imaging (MRI) is diagnostic and visualizes the plaques characteristic of multiple sclerosis.
- A.4.**
- i. *Lhermitte's sign*: Electric shock like sensation down to the back and legs when the neck is flexed which is due to irritated plaque in the cervical cord.
 - ii. *Uthoff's phenomenon*: The disease exacerbates after taking a hot shower which is a transient phenomenon.
- A.5.** These include:
- i. Acute disseminated encephalomyelitis
 - ii. Neuromyelitis optica (Devic's syndrome)
 - iii. Diffuse sclerosis (Schilder's disease)

- iv. Central pontine myelinolysis
- v. Subacute myelo-optic neuropathy (SMON).

A.6. In acute phase, methyl prednisolone 1 gram IV daily for 5 days.

In relapsing and remitting disease, beta interferon is helpful but is very expensive. Other option is glatiramer acetate (Copaxone) 20 mg s/c daily. An oral form is being formulated for convenience. The evidence of benefits from cyclophosphamide, azathioprine, methotrexate, cladribine or mitoxantrone is incomplete. Plasmapheresis enhances no benefits and so is the use of intravenous immunoglobulins.

Spasticity may be treated with baclofen and excessive fatigue must be avoided. Bladder care is a very important step in overall management.

Pseudotumour Cerebri

BRIEF HISTORY

A young girl of 12 was seen in the outpatient department with a history of headaches for the last eight weeks. It started gradually and was accompanied occasionally by vomiting. She was also having spells of dizziness and blurring of vision. For the last two weeks she was complaining of diplopia as well. Other than these symptoms, she was well. There was no history of trauma to the head or serious illnesses in the past.

IMPORTANT CLUES ON CLINICAL EXAMINATION

On examination, she was of good built and looked well. Pulse was 68 per minute, regular and BP was 105/80 mm Hg. General physical examination was normal. Cardiovascular respiratory and abdominal examinations were normal. Her memory and speech was good and there were no abnormality of skull or spine. She had mild weakness of left abducens nerve. All the cranial nerves were intact.

Motor and sensory systems were also intact. Fundoscopic examination revealed blurred optic discs.

INVESTIGATIONS

Following investigations were carried out:

Hb:	12.4 g/dl (normocytic normochromic)	Bicarbonate: 22 mmol/l Chloride: 99 mmol/l Blood urea: 3.2 mmol/l (19 mg/dl)
WBC:	$8.6 \times 10^9/l$ P 62% L 32% M 3% E 3%	Creatinine: 87 $\mu\text{mol/l}$ (0.9 mg/dl) Urine: normal X-ray skull: normal radiological findings.
Platelets:	$320 \times 10^9/l$	

Contd...

Contd...

ESR: 12 mm in 1st hour

Sodium: 136 mmol/l

Potassium: 4.1 mmol/l

QUESTIONS

- Q.1.** What is the most likely diagnosis?
- Q.2.** What investigations are required further?
- Q.3.** What are the findings on lumbar puncture?
- Q.4.** What treatment can be offered for this disease?

ANSWERS

- A.1.** In a young girl with a history of gradual headaches and dizzy spell along with occasional diplopia and papilloedema, the probable diagnosis is increased intracranial pressure due to any cause, i.e., either space occupying lesion or benign intracranial hypertension (pseudotumour cerebri) the latter diagnosis is more appropriate.
- A.2.** These include:
- i. CT scan of brain: This may show a space occupying lesion with or without midline shift or small ventricles in case of pseudotumour cerebri.
 - ii. Ventriculogram: This may show small or normal sized ventricles in pseudotumour cerebri.
- A.3.** The lumbar puncture would reveal raised. The CSF pressure. CSF proteins may be normal or raised and there are no cells either.
- A.4.** Oral glycerol or dexamethasone 6 to 12 mg every six hours can be helpful in lowering the intracranial pressure. Afterwards daily, twice weekly and then weekly lumbar punctures to lower the CSF pressure is advised. Recovery takes place gradually over a period of weeks to months. Diamox (acetohexamide) which is a carbonic anhydrase inhibitor can be used in a dose of 250 mg bd to decrease the CSF production, but serum K^+ levels should be regularly checked. Surgical shunting is another modality of treatment.

Wilson's Disease

BRIEF HISTORY

A 21-year-old man presented to the medical outpatient department with a history of fidgety movements affecting his arms, neck, face and legs along with drooling of saliva, difficulty in swallowing and phonation for the last five years. These symptoms progressed gradually. In addition to this, on quite a few occasions, he became aggressive and had very bizarre behaviour. On two occasions in the past, it was noticed that he had jaundice, but was treated symptomatically by a general practitioner. His birth was without any complications.

IMPORTANT CLUES ON CLINICAL EXAMINATION

On examination, he was restless and had resting tremours and was moving his fingers, neck and head involuntarily in all directions. Saliva was drooling from his mouth. He had dysarthria and his arms and legs showed lead pipe type rigidity. Pulse was 80 per minute and regular and BP was 120/75 mm Hg. Heart sounds were normal and so were respiratory and abdominal examinations. Examination besides above mentioned findings showed no sensory deficit and reflexes were present and plantars were equivocal. Examination of eyes gave a clue to the diagnosis.

INVESTIGATIONS

Following investigations were carried out:

Hb:	13.5 g/dl	Chloride:	96 mmol/l
	(normocytic	Bilirubin:	34 umol/l(2.0 mg/dl)
	normochromic)	SGOT:	102 U/l

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WBC:	8.7 × 10 ⁹ /l	SGPT:	140 U/l
	P:70% L:25%	Albumin:	2.9 g/dl
	M:3% E:2%	Alk Phos:	365 U/l
ESR:	15 mm in 1st hour	Urine:	normal
Sodium:	132 mmol/l	ECG:	normal sinus rhythm
Potassium:	4.8 mmol/l		
Bicarbonate:	22 mmol/l		

QUESTIONS

- Q.1.** What is the diagnosis?
- Q.2.** What is the clue on eye examination?
- Q.3.** What is the mode of inheritance?
- Q.4.** How would you confirm your diagnosis?
- Q.5.** What is the treatment?

ANSWERS

- A.1.** The history of involvement of extrapyramidal system in a young male with derranged liver functions and a clue on eye examination favours a diagnosis of Wilson's disease.
- A.2.** Patients with Wilson's disease show:
- Kayser-Fleischer ring which is due to deposition of copper in Descemet's membrane of cornea.
 - These rings may be accompanied by sunflower cataracts.
- A.3.** Wilson's disease is an autosomal recessive disorder which is caused by abnormality in the hepatic excretion of copper which results in toxic accumulation of copper in the liver, brain (basal ganglia) and other organs also called hepatolenticular degeneration. Basic fault is the deficiency of plasma copper binding protein ceruloplasmin.
- A.4.** It is confirmed as follows:
- Low serum concentration of ceruloplasmin.
 - Increased concentration of copper in liver biopsy.
 - Increased concentration of copper in the urine.
 - Reduced serum concentration of copper.
- A.5.** This consists of removing the copper deposits from the organs as soon as possible. The drug of choice is D-Penicillamine (Vistamin) which is administered orally in an average dose of 1 gram daily before meals. Along with its vitamin B₆ (Pyridoxine) is also given. Important side effects are bone marrow depression and a metallic taste in the anterior two-thirds of tongue. Adjuvant use of steroids is also recommended. Normally, the therapy is continued for the rest of life.
Zinc salt supplements have also been of value in improving the condition.

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Sub-arachnoid Haemorrhage

BRIEF HISTORY

A 62-year-old lady was admitted via the accident and emergency department with a sudden history of collapse and loss of consciousness for three hours. History from the husband revealed that she complained of sudden severe left frontal headache and simply fell on the floor just after getting out of the car. She also had an attack of vomiting consisting of a small quantity of clear fluid. Her breathing became laboured and she had generalised twitching for a few moments which disappeared on its own. In the past history, she had never been ill enough to be in the hospital, but the husband could remember that his wife was told that she was noticed to have high blood pressure three years ago for which she took tablets but not regularly. She did not stick to a low salt diet as advised by her doctor.

IMPORTANT CLUES ON CLINICAL EXAMINATION

On examination, she was found to be comatosed. Her blood pressure was 220/130 mm Hg, pulse was 68 per minute and regular. JVP was not raised and there was no lymphadenopathy. In the cardiovascular system, she had an ejection systolic murmur at the apex radiating to her right side of the neck. Her chest was clear and there were no abdominal findings. She had marked neck stiffness, left-sided ptosis and the left pupil was somewhat dilated and slower to react to light. She had a flaccid paralysis of her right side. On fundoscopic examination, she was found to have marked bilateral AV nipping and a few exudates, but there was no evidence of papilloedema. Reflexes were brisk on the right side with an upgoing plantar.

INVESTIGATIONS

Following were the results of various investigations:

Hb:	11.9 g/dl (normocytic normochromic)	Blood urea:	11.2 mmol/l (67 mg/l)
		Creatinine:	117 umol/l (1.3 mg/dl)
		Blood glucose:	8 mmol/l (144 mg/dl)
WCC:	$8 \times 10^9/l$ P:80% L:18% M:2%	ECG:	normal sinus rhythm, no evidence of infarction
ESR:	30 mm in 1st hour	Chest X-ray:	heart size moderately enlarged. No active lung lesion was seen.
Sodium:	140 mmol/l		
Potassium:	3.4 mmol/l		
Bicarbonate:	26 mmol/l		
Chloride:	101 mmol/l		

QUESTIONS

- Q.1. What is your most likely diagnosis, and why?
- Q.2. How do you explain her ptosis?
- Q.3. What is the prognosis?
- Q.4. Name two most important investigations.
- Q.5. Name one drug which is used in this condition.

ANSWERS

- A.1.** The most likely diagnosis in this lady is subarachnoid haemorrhage. History of previous hypertension, sudden onset of symptoms with headache and finding of neck stiffness and rapid deterioration in consciousness all suggest this diagnosis. Subarachnoid haemorrhage is not always associated with occipital headache.
- A.2.** Probably, an aneurysm at the junction of the posterior communicating artery and posterior cerebral artery pressing on the third nerve nucleus is the explanation for ptosis in this patient.
- A.3.** The prognosis in most patients of subarachnoid haemorrhage presenting with coma is very poor. This also depends on the age of the patient and any serious underlying pathology.
- A.4.** i. CT scan of the brain: It will show blood in the ventricles. If there is no cerebral oedema, one can go ahead with a lumbar puncture which shows homogeneously blood stained CSF.
- ii. Carotid angiography: To find any more aneurysmal malformation but it should be performed after 7 to 10 days because before that the bleeding site is in spasm, so one cannot outline the leaking aneurysm if surgical intervention is required. However, this strategy is not followed by some neurosurgeons.
- A.5.** Nimodipine (Nimotop) which is given orally in dose of 60 mg four hourly for 21 days. It is a calcium channel blocker and relieves spasm of normal cerebral blood vessels so, that the perfusion of the normal brain tissue is not jeopardised.

*Myasthenia Gravis***BRIEF HISTORY**

A 50-year-old man was admitted with a six-months history of generalised weakness double vision and difficulty in swallowing with weight loss. His difficulty in swallowing and tiredness on chewing was getting progressively worse and he had recently started avoiding solid foods almost altogether and had lost 4 kg in weight over the last two months. Double vision was not persistent, but he experienced it almost everyday for the last four weeks. On direct questioning, he also admitted that he felt excessively tired and weak in his arms while combing his hair and this used to get worse in the evening. There was no history of cough, expectoration, chest pain or palpitation. His bowels were regular. His son told that his father's speech was becoming more nasal and fluids used to regurgitate from his nose.

IMPORTANT CLUES ON CLINICAL EXAMINATION

General physical examination was unremarkable with no swelling in the neck. He had bilateral ptosis, pupil size was normal on both sides with normal light and accommodation reflexes, but he had diplopia on looking to the left. Fundi were normal. Motor, sensory systems and reflexes were normal. Rest of the systemic examination was normal, too.

INVESTIGATIONS

Following were the results of various investigations:

Hb:	13.4 g/dl	Potassium:	3.4 mmol/l
	(normocytic	Bicarbonate:	25 mmol/l
	normochromic)	Chloride:	100 mmol/l

Contd...

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WCC:	9 × 10 ⁹ /l	Blood sugar:	6.7 mmol/l (121 mg/dl)
	P:76% L:20%	Blood urea:	5 mmol/l (30 mg/dl)
	M:2% E:2%	Creatinine:	84 umol/l (0.9 mg/dl)
Platelets:	260 × 10 ⁹ /l	ECG:	normal
ESR:	14 mm in 1st hour		
Sodium:	139 mmol/l		

QUESTIONS

- Q.1.** What is the most likely diagnosis?
- Q.2.** Give three investigations to help the diagnosis.
- Q.3.** Give one more investigation that you would like to include.
- Q.4.** What is myasthenic syndrome?
- Q.5.** Name three drugs that may help this patient.

ANSWERS

- A.1.** The most likely diagnosis in this man with diplopia, difficulty in chewing his food and undue tiredness and weakness especially in the later hours of the day, is myasthenia gravis.
- A.2.**
- i. Tensilon test (Edrophonium hydrochloride) 10 mg IV slowly improves the muscle power quite well.
 - ii. Electromyography(EMG)—Decremental response to low frequencies (3 per second) of nerve stimulation. This is positive in 95 percent of cases. Single fiber EMG is also helpful.
 - iii. Antibody screening test (Anti acetylcholine receptor and anti-striated muscle antibodies).
- A.3.** A chest X-ray (to look for thymus enlargement).
- A.4.** Myasthenic syndrome is characterised by weakness of muscles as seen in true myasthenia gravis, but it is almost always associated with underlying malignancy. The syndrome is also known as Eaton-Lambert syndrome. Characteristic post-tetanic potentiation seen on electromyography helps to differentiate this syndrome from true myasthenia gravis.
- A.5.** Drugs that may help this patient are:
- Neostigmine
 - Pyridostigmine
 - Corticosteroids.

However, thymectomy does help in improving the condition whether there is a thymoma or not. In addition to the above, in acute phase, intravenous immunoglobulins (IVIG) or plasmapheresis have proven to be beneficial.

*Paget's Disease***BRIEF HISTORY**

A 65-year-old man attended the outpatient department with six-month history of pain in the left thigh and hip. He also mentioned that he was getting undue shortness of breath and swelling of feet. He also had headaches off and on and his son told that for the last four months, he was becoming hard of hearing. There was no history of trauma, hypertension or ischaemic heart disease. He was not a diabetic either. He smoked 6 to 10 cigarettes a day.

IMPORTANT CLUES ON CLINICAL EXAMINATION

On examination, he was uncomfortable. Temperature was normal. There was pitting oedema on both ankles. Pulse was 110 per minute, regular and collapsing in character. BP was 150/60 mm Hg. Heart sounds were normal with no added sounds. Chest revealed bilateral basal crackles. Abdominal examination was normal. There was some element of conduction deafness on testing the cranial nerves. The right thigh was a bit swollen, tender and warm as compared to left thigh.

INVESTIGATIONS

Investigations included:

Hb:	13.5 g/dl (normocytic normochromic)	Blood sugar	5.8 mmol/l (104 mg/dl)
		Blood urea	7 mmol/l (42 mg/dl)
		Creatinine	103 μ mol/l (1.1 mg/dl)
WCC:	$8.7 \times 10^9/l$	Bilirubin:	16 μ mol/l (0.9 mg/dl)
	P:74% L:22%	Alk.Phos:	780 U/l
	M:3%E:1%	SGOT (AST):	23 U/l

Contd...

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Platelets:	340 × 10 ⁹ /l	SGPT (ALT):	34 U/l
ESR:	15 mm in 1st hour	Urine:	normal
Sodium:	138 mmol/l	ECG:	sinus tachycardia, T
Potassium:	4.6mmol/l		wave inverted in the
Bicarbonate:	23 mmol/l		lateral chest leads.
Chloride:	98 mmol/l	X-ray	
		right femur:	as shown in Figure 47.1



Fig. 47.1: X-ray right femur

QUESTIONS

- Q.1. What is the diagnosis?
- Q.2. Describe the X-ray of femur.
- Q.3. What are pseudofractures and how would you distinguish it radiologically from fissure fractures?
- Q.4. What are the urinary markers of this disease?
- Q.5. Describe a few complications of this disease.
- Q.6. What treatment can be offered?

ANSWERS

- A.1.** In a 65-year-old patient with a history of pain in the thigh bone (femur), deafness, a wide pulse pressure and collapsing pulse with a raised alkaline phosphatase and normal transaminases and bilirubin indicates a diagnosis of Paget's disease of bone.
- A.2.** The X-ray shows thick, irregular cortex and narrowed medullary canal with a lot of trabeculations and abnormal curvature of the femur. Small transverse fracture lines are also visible on the convexity which are called stress or fissure fractures.
- A.3.** The pseudo fractures are also called Looser's zones which occur in osteomalacia, but they are present on the medial side of the bones and are symmetrical, while fissure fractures are present on the lateral side and are asymmetrical.
- A.4.** The urine contains hydroxyproline reflecting increase bone resorption. Urinary calcium is also increased if the patient is immobilized. Increased excretion of pyridinium cross link pyridinoline is a better indicator of bone resorption than excretion of hydroxyproline as former is more specific component of bone matrix than the latter.
- A.5.**
- i. Severe bone pain.
 - ii. Pathological fractures.
 - iii. High output cardiac failure.
 - iv. Deafness due to direct pagetic involvement of ossicles, bone of cochlea or impingement on the VIII cranial nerve due to narrowing of the auditory foramen.
 - v. Urinary stone formation especially containing calcium.
 - vi. Sarcoma-incidence is less than one percent and the commonest site is femur, humerus, skull, pelvis and vertebrae in that order. Although majority are osteosarcoma, but fibrosarcoma and chondrosarcoma may also occur.
- A.6.** Most patients require no treatment as they have no symptoms and disease is diagnosed incidentally. Indications for therapy include persistent pain, neural compression, deformity, high output cardiac failure, hypercalcaemia and severe hypercalciuria.

- i. Aspirin is effective analgesic and up to four grams per day can be given.
- ii. Indomethacin or other non-steroidal anti-inflammatory drugs are also used.
- iii. Steroids can also be used but in large doses and, therefore, side effects are important to be aware of.
- iv. Sodium fluoride (80-120 mg per day) for a year or so may help ameliorating the symptoms.
- v. Calcitonin has been administered and it improves the pain and decreases levels of alkaline phosphatase. Its dose is 50 IU thrice weekly sc or im. Nasal spray is also available and is equally effective, but it is quite expensive.
- vi. Mithramycin which is an antibiotic drug has also been used and produces striking decrease in urinary hydroxyproline excretion. Dose is 10 to 15 micrograms/kg IV daily for ten days.
- vii. Gallium nitrate inhibits bone resorption by inhibiting the ATP-dependent proton pump of osteoclasts.

Diphosphonates: Disodium etidronate 5 mg/kg daily for 3 to 12 months between meals to increase absorption. Remission is induced up to two years. Others include pamidronate, alendronate, clodronate, tiludronate, etc. Currently alendronate and ibandronate, are used though experimental, but they are the most potent diphosphonates. Alendronate (Fosamax) is also available in weekly dosage of 70 mg. Pamidronate (Aredia) can be given as 30 mg once a week for six weeks or 30 mg on the first week and then 60 mg every other week up to total dose of 210 mg. Its maximum dose is 360 mg per treatment session in divided dosage. The course may be repeated after six months. Tiludronic acid (Skelid) is given as 400 mg once daily for twelve weeks and is repeated after six months. In Paget's disease excessive calcium supplements should be avoided.

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Polymyositis

BRIEF HISTORY

A 45-year-old man was admitted in the hospital with a six-week history of inability to walk, talk, swallow and move his upper limbs. The weakness was first to occur and was gradual in onset and it affected his thighs and shoulders more severely than his hands and feet and they were also painful on movement. Two weeks after this, he felt difficulty in swallowing and his speech became nasal as well. There was no history of any febrile illness and he was not a known hypertensive or diabetic. There was no history of drug intake and no member of his family suffered from such disorder. He was married, had five children and they were all healthy. He smoked 25 cigarettes a day.

IMPORTANT CLUES ON CLINICAL EXAMINATION

On examination, he looked anxious and there was generalised wasting of the muscles. Pallor was obvious. He could hardly speak and saliva was dribbling from his mouth. Temperature was 99°F, pulse was 80 per minute and heart sounds were normal. BP was 130/85 mm Hg. Chest expansion was poor bilaterally and there was a constant wheeze on the left midzone of the chest. Abdominal examination was unremarkable. Nervous system revealed intact higher mental functions and cranial nerves. Sensory system was intact but muscle power was of grade 0 proximally and grade I distally. Tendon reflexes were diminished and plantars were downgoing. No fasciculations were visible. All the sphincters were intact. There were no signs of meningeal irritation. Both fundi were normal.

INVESTIGATIONS

Investigations included:

Hb:	12.5 g/dl (normocytic normochromic)	Blood sugar:	6 mmol/l (108 mg/dl)
		Blood urea:	5 mmol/l (30 mg/dl)
WCC:	$9.2 \times 10^9/l$ P:72% L:20% M:2% E:6%	Creatinine:	108 $\mu\text{mol/l}$ (1.2 mg/dl)
		LFT's:	normal
Platelets:	$270 \times 10^9/l$	CPK:	5820 U/l
ESR:	85 mm in 1st hour	Urine:	normal
Sodium:	139 mmol/l	ECG:	sinus rhythm, no evidence of acute ischaemia
Potassium:	4 mmol/l	Chest X-ray:	as shown in Figure 48.1
Bicarbonate:	24 mmol/l		
Chloride:	100 mmol/l		



Fig. 48.1: Chest X-ray

QUESTIONS

- Q.1. What is the diagnosis?
- Q.2. What are the three confirmatory investigations?
- Q.3. Is chest X-ray findings significant in this case?
- Q.4. How does this condition involve skin?
- Q.5. What is the treatment?

ANSWERS

- A.1. In a male who has a history of muscle weakness which started proximally and the muscles were also tender and then there was quadriplegia with inability to swallow and phonate with a CPK of more than 5000 U/l leads to a diagnosis of primary muscle disorder most probably polymyositis.
- A.2. Besides CPK which is in thousands, serum aldolase is also important. Others include an electromyogram (EMG) which usually shows multiphasic potentials and muscle biopsy which indicates degenerated and fibrosed muscles with infiltration of small lymphocytes.
- A.3. Yes, polymyositis may be associated with underlying malignancy and bronchogenic carcinoma is one of them.
- A.4. If the skin is also involved, then it is called dermatomyositis. This is characterised by classical heliotropic rash around the eyes and thick knuckle pads called Gottron's sign.
- A.5. The mainstay of therapy is corticosteroids which are given in large doses (80 mg/day) and continued for at least 2 to 3 months, then gradual reduction, over next 6 to 12 months should be considered and then the patient is kept on a maintenance dose. Other immunosuppressive therapy can be continued in the form of azathioprine although cyclophosphamide has also been used. Plasmapheresis is another form of treatment, but it is quite expensive and should be instituted as early as possible.

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Osteoporosis

BRIEF HISTORY

A 70-year-old lady was admitted in the hospital through out-patient department with a one-week history of severe low back ache which was intolerable and was more while bending down or walking briskly. There was no radiation of pain and it did not get worse on sneezing or coughing. She saw a local general practitioner who prescribed some nonsteroidal anti-inflammatory medicines and a sleeping pill. There was no history of lifting heavy things or injury to the back. However, the treatment which she had did not relieve her pain and she was still restless and in agonising pain, especially while lying down and turning her position in the bed or getting out of it. She was not a known diabetic or hypertensive. There was no history of weight loss, fever, night sweats or cough.

IMPORTANT CLUES ON CLINICAL EXAMINATION

On examination, she appeared to be in pain. There was no anaemia, clubbing or lymphadenopathy. JVP was not raised. She had bilateral osteoarthritis of her knees. There was kyphoscoliosis and some tenderness over her T₁₂-L₁ region on the back was elicited. Straight leg raising test was normal. Abdominal, respiratory and cardiovascular systems were normal. Cranial nerves were intact, motor and sensory systems were normal. She had absent left ankle jerk with loss of sense of vibration. All other tendon reflexes were normal with bilateral downgoing plantars.

INVESTIGATIONS

Following were the results of various investigations:

Hb:	13.4 g/dl (normocytic normochromic)	Calcium:	2.25 mmol/l
		Blood urea:	8 mmol/l (48 mg/dl)
WCC:	$8.7 \times 10^9/l$ P:60% L:35% M:4% E:1%	Creatinine:	140 $\mu\text{mol/l}$ (1.6 mg/dl)
		Blood sugar:	7.1 mmol/l (128 mg/dl)
Platelets:	$300 \times 10^9/l$	Alk Phos:	70 u/l
		Urine:	normal
		ECG:	normal
ESR:	29 mm in 1st hour	X-ray-dorso-	
Sodium:	142 mmol/l	lumbar spine:	crush fracture L ₁₋₂
Potassium:	4.1 mmol/l		vertebrae with
Bicarbonate:	25 mmol/l		increased translucency
Chloride:	97 mmol/l		of bones.

QUESTIONS

- Q.1.** What is the most likely diagnosis?
- Q.2.** What three further investigations will you ask for?
- Q.3.** Why did rest and immobilisation fail to help this patient?
- Q.4.** What are the endocrine causes of this diagnosis?
- Q.5.** Briefly outline the management of this disorder.

ANSWERS

- A.1.** The most likely diagnosis in this lady with sudden severe backache which was made worse by movements of her back with no radiation, not controlled by milder analgesics, kyphoscoliosis, tenderness over T₁₂.L₁ region and normal serum calcium, phosphorus, and alkaline phosphatase with crush fracture of T₁₂ vertebra and increased bony translucency is osteoporosis. The absence of vibration sense and ankle jerk is not uncommon in people who are above sixty years of age.
- A.2.**
- i Immunoglobulin electrophoresis (to rule out multiple myeloma).
 - ii Trephine biopsy of the bones for histological confirmation of the diagnosis.
 - iii Bone Densitometry (DXA scanning) for screening people and monitoring effects of treatment.
- A.3.** Rest and immobilisation contribute to further loss of bone density. Patients must always be encouraged to maintain their mobility with adequate pain control.
- A.4.**
- i Hyperthyroidism
 - ii Cushing's syndrome
 - iii Acromegaly
 - iv Diabetes mellitus.
- A.5.** The general measures include a little rest, local heat, adequate analgesia and avoidance of constipation. Gradual mobilization is also desired. Oestrogens and androgens also help to slow down the process. Oestrogens act by decreasing the rate of bone resorption, especially in menopausal women. Androgens in the form of anabolic steroids are weaker and they have no advantage to be used in women. Oestrogen therapy may increase incidence of endometrial carcinoma in postmenopausal women.
- Calcium preparations are also beneficial. Vitamin D also plays an important role in preventing osteoporosis.
- Fluoride also increases new bone formation, but its use is not widely recommended.
- It has been suggested that if the dose of fluoride is 25 mg per day and calcium is given in 1 gram per day with vitamin

D 50,000 units twice weekly, then new bone formation occurs.

Calcitonin and diphosphonates have shown no benefits except control of pain. Use of growth hormone is not beneficial either.

Bisphosphonates work by inhibiting osteoclast induced bone resorption. Special precautions are observed for administration of these drugs. All patients should receive oral supplements of calcium and vitamin D as well. They are also effective in preventing corticosteroid induced osteoporosis and treatment is indicated if a person is using at least 7.5 mg daily for more than three months.

Selective oestrogen receptor modulators (SERM's) can be used by postmenopausal women in place of oestrogens. Raloxifene (Evista) 60 mg daily for six months is widely used. It, however, increases the risk of thromboembolism and should not be used by women with such history.

Idiopathic Thrombocytopaenic Purpura

BRIEF HISTORY

A 36-year-old woman presented to the accident and emergency department with a history of nose bleed which could not be stopped by ordinary measures. Two days before this, she had scaling of teeth by a dentist but bleeding from gums continued for a few hours. There were no other symptoms or complaints. However, she gave history of a flu-like illness ten days ago with sore throat and it subsided in two days with paracetamol. There was no history of bleeding from any other site and there was no significant family history either.

IMPORTANT CLUES ON CLINICAL EXAMINATION

On examination, she looked anxious and the blood was dribbling from the right nostril. Her pulse was 98 per minute and regular, while the blood pressure was 130/80 mmHg. She was afebrile and there was no lymphadenopathy either. She had a large ecchymosis on her left arm and a few petechiae on her shins, thighs and abdomen.

INVESTIGATIONS

Investigations included the following:

Hb:	13 g/dl (normocytic normochromic)	Chloride:	99 mmol/l
		Blood sugar:	6 mmol/l (108 mg/dl)
		Blood urea:	5.6 mmol/l (33 mg/dl)
WCC:	$7 \times 10^9/l$ P:72% L:24% M:2% E:2%	Creatinine:	117 μ mol/l (1.3 mg/dl)
		LFT's:	normal
		Urine:	blood++
Platelets :	$17 \times 10^9/l$	ECG:	sinus rhythm

Contd...

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ESR:	15 mm in 1st hour	Chest X-ray:	normal
Bilirubin:	2.6 mg/dl		
Sodium:	138 mmol/l		
Potassium :	3.4 mmol/l		
Bicarbonate:	24 mmol/l		

QUESTIONS

- Q.1.** What is the most likely diagnosis?
- Q.2.** What is the differential diagnosis?
- Q.3.** What further two investigations you would ask for?
- Q.4.** Discuss briefly the management.

ANSWERS

- A.1.** A patient with the history of flu-like illness in the recent past and then followed by bleeding from gums and nose with ecchymosis and petechiae, a normal haemoglobin, WCC but a low platelet count is most likely to have idiopathic thrombocytopaenic purpura (ITP).
- A.2.** Generally, the diagnosis is straight forward, however, ITP should be differentiated from:
- i. Drug induced thrombocytopaenia, e.g., quinine in tonic water or to any other drug to which the patient is sensitive.
 - ii. Autoimmune disorders especially systemic lupus erythematosus (SLE) and other connective tissue disorders (presence of anticardiolipin antibodies). Other disorders include autoimmune thyroiditis, hyperthyroidism, etc.
 - iii. Associated with autoimmune haemolytic anaemias called Evans' syndrome when there is neutropaenia as well.
 - iv. Chronic lymphatic leukaemia (CLL). It is though rare at this age, acute lymphoblastic leukaemia is more probable.
 - v. Associated with solid tumours
 - vi. HIV associated infections.
 - vii. Acute infections, e.g., rubella, mumps, chickenpox, glandular fever, CMV, herpes and acute and chronic infections.
- A.3.** These investigations include:
- i. ANA and anti-double stranded DNA antibodies to rule out systemic lupus erythematosus (SLE).
 - ii. Bone marrow biopsy: It shows normal erythropoiesis and myelopoiesis. Megakaryocytes are increased in number both mature and immature forms.
- A.4.** The management depends on:
- i. degree of thrombocytopaenia
 - ii. severity or risk of a major bleed.

The aim is to increase the circulating platelets and to decrease the antiplatelet antibodies. Corticosteroids are the

mainstay of treatment i.e. 0.5-1.0 mg/kg/day or pulse therapy ie methylprednisolone (Solumedrol) 1 gm diluted in 100 mls of N. saline and infused over one hour daily for five days.

High doses of IV immunoglobulins (0.4 g/kg/day) for 3 to 5 days is also effective.

Immunosuppressant therapy with cyclophosphamide, azathioprine and interferon may be helpful.

Plasmapheresis is also useful to remove anti-platelet antibodies from the blood.

If the disease does not settle with all the above modalities, then splenectomy should be considered.

NB: After splenectomy, the patient is prone to develop recurrent bacterial infections, especially pneumococcal. Therefore, polyvalent pneumococcal vaccine called pneumovax II, 0.5 ml subcutaneous or intramuscular is given. It is directed against 23 most prevalent strains of pneumococcus. This gives adequate immunity for at least six years. Headaches, fever lymphadenopathy, arthralgia, skin rash or serum sickness like symptoms may be encountered as side effects of pneumovax II.

Myelofibrosis

BRIEF HISTORY

A 62-year-old male presented to the medical outpatient department with a four week history of shortness of breath, easy fatigueability and a dragging sensation in the upper left quadrant of his abdomen. This distressed him a great deal and one week prior to his present appointment, he felt severe pain in that part of abdomen, but he got better with some analgesics by a local doctor. He was also complaining of itching all over the body. There was no such family history and he had been well in the past.

IMPORTANT CLUES ON CLINICAL EXAMINATION

On examination, he looked wasted and pale. There were scratch marks on his abdomen and back of the chest but no lymphadenopathy. The pulse was 100 per minute and regular, BP was 115/85 mmHg. Heart sounds were normal, but there was a low grade ejection systolic murmur at the precordium. Abdominal examination revealed a huge spleen about 15 cm below the left subcostal margin. The respiratory and neurological examinations were normal.

INVESTIGATIONS

Following investigations were carried out:

Hb :	6.4 g/dl (poikilocytes, tear drop cells occasional nucleated RBCs)	Bicarbonate:	24 mmol/l
		Chloride:	102 mmol/l
		Blood urea:	6 mmol/l (36 mg/dl)
WCC:	$14.6 \times 10^9/l$	Blood sugar:	6.4 mmol/l (115 mg/dl)
	P:80% L:18%	Creatinine:	200 umol/l (2.2 mg/dl)
	metamyelocytes: 2%	Urine:	normal

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Platelets:	$450 \times 10^9/l$	ECG:	normal sinus rhythm.
ESR:	75 mm in 1st hour	Chest X-ray:	heart enlarged, bilateral pulmonary congestion.
Sodium:	136 mmol/l		
Potassium:	3.4 mmol/l		

QUESTIONS

- Q.1. What is the most likely diagnosis?
- Q.2. What further investigations will help the diagnosis?
- Q.3. Discuss the differential diagnosis.
- Q.4. Name a few complications of this disorder.
- Q.5. What treatment could be offered?

ANSWERS

A.1. In a patient who has a history of weight loss, pallor and massive splenomegaly with haematological evidence of anaemia, leukocytosis and thrombocytosis, the most likely diagnosis is a myeloproliferative disorder: myelofibrosis or myelosclerosis.

A.2. These are:

- i. *Bone marrow examination* It yields a dry tap. A needle or open biopsy shows extensive fibrosis with islands of haemopoietic cells and megakaryocytic hyperplasia.
- ii. *Serum uric acid* Which is usually elevated.
- iii. *Leukocyte alkaline phosphatase score (LAP)* It is usually elevated but may be normal or even low. It is also called LAP scoring.
- iv. *Ferrokintic studies* Although it is rarely necessary but may be useful to know the extent of the disease, especially in cases where splenectomy is being considered.
- v. Philadelphia chromosome is absent.

A.3. This should be differentiated from:

- i. Chronic myeloid leukaemia: The bone marrow shows predominance of myelocytes and promyelocytes, and leukocyte alkaline phosphatase (LAP) is low and Philadelphia chromosome is present.
- ii. Polycythaemia vera: The haemoglobin is very high, LAP is also raised and the ESR is less than 1 mm in 1st hour.
- iii. Secondary myelosclerosis: Hodgkin's disease, granulomatous disease, e.g. sarcoidosis, tuberculosis.

A.4. They can be divided into:

A. Major complications:

- i. Hypersplenism.
- ii. Splenic infarctions.
- iii. Splenic rupture.
- iv. Acute myeloblastic leukaemia.

B. Minor complications:

- i. Secondary gout (20%).

- ii. Secondary platelet deficiency.
 - iii. Peptic ulceration.
 - iv. Chronic loss of blood in the gastrointestinal tract.
 - v. Bruising and haematoma.
- A.5.** There is no definite treatment.
- i. Different deficiencies should be corrected, e.g. folic acid.
 - ii. Regular blood transfusions should be started.
 - iii. Splenic irradiation and chemotherapy to reduce size of spleen.
 - iv. Busulphan, hydroxyurea or chlorambucil are widely used.
 - v. Allopurinol is also supplemented.
 - vi. Role of splenectomy is controversial but is advisable if severe anaemia and thrombocytopenia persist.

Polycythaemia

BRIEF HISTORY

A man of 60 was admitted with a six hour history of right-sided weakness and dysphasia. This had come on slowly and there was no history of headache or loss of consciousness.

He had been seen in accident and emergency department twice in the last six months with transient ischaemic attacks, but since he recovered quickly, he was not hospitalised on either occasion. There were no other symptoms except that he complained in the recent past of undue itching, especially after bathing. He smoked 20 cigarettes a day. There was no history of hypertension or diabetes mellitus.

IMPORTANT CLUES ON CLINICAL EXAMINATION

On examination, he had expressive dysphasia but did not appear to be confused. Blood pressure was 150/80 mmHg. Pulse 80 per minute and regular. No clubbing or oedema was noticed. Thyroid and lymph nodes were not enlarged. He was in sinus rhythm with no heart murmurs. There were no carotid bruits either. Respiratory system was normal. His liver was 2 cm enlarged, firm and non-tender, spleen was 4 cm enlarged. There was no ascites. Neurological examination confirmed an upper motor neurone lesion affecting his right side, increased tendon reflexes and an upgoing right plantar. Fundi revealed engorged blood vessels only.

INVESTIGATIONS

Investigations were reported as follows:

Hb :	19.9 g/dl	Chloride:	101 mmol/l
	(normocytic	Blood glucose:	6.8 mmol/l (112 mg/dl)
	normochromic)		

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WCC	15 × 109/l	Blood urea:	9.3 mmol/l (56 mg/dl)
	P: 74% L: 20%	Creatinine:	122 µmol/l (1.4 mg/dl)
	M: 4% E: 2%	Protein:	7.2 g/dl
Platelets :	620 × 109/l	Albumin:	3.6 g/dl
ESR:	1 mm in 1st hour	Bilirubin:	17 µmol/l (1.0 mg/dl)
Sodium:	140 mmol/l	Urine:	normal
Potassium :	4 mmol/l	Chest X-ray:	within normal limits
Bicarbonate:	40 mmol/l		

QUESTIONS

- Q.1.** What is the most likely diagnosis?
- Q.2.** What three further investigations will help this diagnosis?
- Q.3.** Name four therapeutic agents which are known to be helpful in the treatment.
- Q.4.** Name five complications of this disease.

ANSWERS

- A.1.** The most likely diagnosis in this man with history of previous transient ischaemic attacks and now presenting with a completed stroke, hepatosplenomegaly, high Hb, high white cell and platelet count and low ESR is polycythaemia vera. The onset of this condition is usually insidious and it is more common in males.
- A.2.**
- i. Red cell mass estimation.
 - ii. Leukocyte alkaline phosphatase (LAP) scoring.
 - iii. Bone marrow aspiration and trephine biopsy.
- A.3.**
- i. Radioactive phosphorus.
 - ii. Busulphan.
 - iii. Hydroxyurea.
 - iv. Chlorambucil.
- A.4.**
- i. Thrombosis.
 - ii. Haemorrhage.
 - iii. Hyperuricaemia and gout.
 - iv. Myelofibrosis.
 - v. Leukaemia.

Pernicious Anaemia/SACDC

BRIEF HISTORY

A 59-year-old lady was admitted with a two-month history of confusion, unsteady gait and falls. During the week preceding her admission, she had three falls. She had no loss of appetite or weight. There were no urinary or bowel symptoms. She was not a known hypertensive or diabetic and was taking no medications.

IMPORTANT CLUES ON CLINICAL EXAMINATION

On examination, she was moderately confused and disorientated. Blood pressure was 140/75 mmHg. Pulse was 88 per minute and regular. JVP was not raised and there was no poedal oedema. There was no thyroid or lymph node enlargement, clubbing or tremours. She looked slightly icteric. Respiratory system was normal. Her spleen was 2 cm enlarged, but there was no hepatomegaly or ascites. The heart sounds were normal, but she had an apical ejection systolic murmur. Cranial nerves and fundi were normal. There were no signs of meningeal irritation. Power and tone were reduced in both legs with absent ankle jerks bilaterally and both plantars were upgoing. Touch, pain and vibration sensations were impaired below the knee on both sides. Clinically, there were no signs of fracture of both hips.

INVESTIGATIONS

Following were the results of various investigations:

Hb :	5.1 g/dl (MCV 112 fl)	Blood glucose:	4.0 mmol/l (72 mg/dl)
WCC:	$3.5 \times 10^9/l$	Blood urea:	6.4 mmol/l (38 mg/l)
	P: 74% L: 20%	Creatinine:	90 μ mol/l (1.0 mg/dl)
		Protein:	6.3 g/dl

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	M: 4% E: 2% (hypersegmented polys with shift to the right)	Albumin: Bilirubin: Urine: ECG:	3.6 g/dl 18 umol/l (1.1 mg/dl) normal showed anterolateral ischaemia only.
Platelets :	270 × 10 ⁹ /l	Chest X-ray:	within normal limits
ESR:	39 mm in 1st hour		
Sodium:	140 mmol/l		
Potassium :	3.8 mmol/l		
Bicarbonate:	23 mmol/l		
Chloride:	99 mmol/l		

QUESTIONS

- Q.1.** What is the most likely diagnosis?
- Q.2.** Name a few causes of reversible dementia.
- Q.3.** How do you explain the presence of jaundice?
- Q.4.** Name one other serious complication of your final diagnosis.
- Q.5.** Name other diseases associated with this condition.
- Q.6.** What three investigations will help the diagnosis?

ANSWERS

- A.1.** The diagnosis in this lady, who presented with confusion, unsteadiness of gait, falls, mild jaundice, splenomegaly, pyramidal and posterior column signs with low Hb, and hypersegmented neutrophils is B₁₂ (probably pernicious anaemia) with subacute combined degeneration of the cord.
- A.2.** i. Pernicious anaemia.
ii. Myxoedema.
iii. Phenytoin toxicity.
iv. Alcoholism.
- A.3.** Reticulocytosis with variable degree of haemolysis is commonly seen in many cases with pernicious anaemia. Mild jaundice in these patients, therefore, is a result of haemolysis.
- A.4.** Besides subacute combined degeneration of the cord, carcinoma of the stomach is a recognised complication.
- A.5.** These include mostly diseases of autoimmune origin, e.g. Graves' disease, myxoedema, thyroiditis, idiopathic adrenocortical insufficiency, vitiligo, diabetes and hypoparathyroidism. About 90 percent of the patients suffering from pernicious anaemia have antiparietal cell antibody and 60 percent have anti-intrinsic factor antibody.
- A.6.** i. Serum B₁₂ and folate level: Radio-immuno-assay is useful technique. Normal B₁₂ is 200 to 900 pg/ml. Values less than 100 pg/ml indicate significant deficiency. Normal folic acid values range from 6 to 20 ng/ml. Values less than 4 ng/ml are diagnostic of folate deficiency.
- ii. Bone marrow aspiration: Bone marrow is hypercellular with a decrease myeloid:erythroid ratio and abundant stainable iron. There is nuclear-cytoplasmic asynchrony.
- iii. Schilling's Test: This is performed to know the pathogenesis of pernicious anaemia. This test is done in three stages:
Stage I An intramuscular injection of 1mg of unlabelled B₁₂ is

given and this is followed shortly by radioactive vitamin B₁₂ orally. Excretion in the urine is measured.

Stage II The patient is given labelled vitamin B₁₂ bound to intrinsic factor. If the patient has pernicious anaemia, then the absorption of B₁₂ approaches normal. If still it is low, then third stage is performed.

Stage III The patient is given antibiotic (to treat blind loop syndrome) and the test is performed. If the excretion of radiolabelled B₁₂ becomes normal in the urine, this means that patient had bacterial overgrowth which resulted in malabsorption of vitamin B₁₂.

*von Willebrand's Disease***BRIEF HISTORY**

A young girl presented to accident and emergency department complaining of a nose bleed which could not be controlled by pinching the nose. She also had nose bleeds in the past and mentioned about easy bruising of the skin. On asking menstrual history, she admitted excessive loss of blood during menstruation. No other family member had similar complaints. She was taking no medicines and was not allergic to any drugs.

IMPORTANT CLUES ON CLINICAL EXAMINATION

On examination, she looked pale, pulse was 110 per minute and regular and BP was 105/75 mmHg. She had two large bruises—one over her right forearm and the other on her left shin. Cardio-vascular, respiratory and abdominal examinations were normal. Central nervous system examination was unremarkable.

INVESTIGATIONS

Following investigations were performed:

Hb:	10.2 g/dl	Bicarbonate:	25 mmol/l
	(microcytic hypochromic)	Chloride:	99 mmol/l
WBC:	$7.5 \times 10^9/l$	Blood glucose:	4.8 mmol/l (86mg/dl)
	P: 76% L: 18%	Blood urea:	5.0 mmol/l (30 mg/l)
	M: 4% E: 2%	Creatinine:	110 μ mol/l (1.2mg/dl)
Platelets:	$300 \times 10^9/l$	Urine:	normal
ESR:	25 mm in 1st hour	Bleeding time:	prolonged
Sodium:	140 mmol/l	Prothrombin time:	normal
Potassium:	3.9 mmol/l		

QUESTIONS

- Q.1.** What is the diagnosis?
- Q.2.** What investigations would confirm your diagnosis?
- Q.3.** What is the mode of inheritance?
- Q.4.** What treatment can be offered?

ANSWERS

- A.1.** For this girl with a history of episodes of recurrent bleeding and a normal prothrombin time with a prolonged bleeding time, the diagnosis is a bleeding disorder most probably von Willebrand's disease.
- A.2.**
- i. Measurement of factor VIII-C level which are low.
 - ii. Measurement of factor VIII R: Ag which are reduced.
 - iii. Reduction of factor VIII: WF by utilizing semi quantitative test based on its co-factor activity for platelet aggregation by antibiotic ristocetin.
- A.3.** It is inherited as an autosomal dominant trait. An autosomal recessive form is also present. von Willebrand factor is absent or deficient. von Willebrand factor is essential for adhesion of platelets, with the injured vessel wall, and secondly it combines with factor VIII-C giving stability to factor VIII-C, otherwise in von Willebrand disease, the half life of factor VIII-C is very much reduced.
- A.4.** Mostly it is supportive therapy. Replacement of factor VIII at regular intervals is important. Antifibrinolytic agent, i.e. tranexamic acid may be useful in menorrhagia.
- Infusion of fresh plasma or cryoprecipitates results in immediate rise in plasma factor VIII activity.

Multiple Myeloma

BRIEF HISTORY

A 70-year-old male presented to the emergency room with a one week history of cough with purulent sputum, fever spiking up to 104°F and diffuse aches and pains, especially severe sharp pain in the chest on coughing. There was no history of haemoptysis. He also complained that for the last three days, he had severe pain in his low back radiating to the left knee which made him totally bedridden. He has had no past medical problem. He smoked 20 cigarettes per day and used to walk 3 kilometers daily. Lately, he was unable to complete his walk due to fatigue and undue breathlessness and excruciating pain.

IMPORTANT CLUES ON CLINICAL EXAMINATION

On examination, he looked pale. His temperature was 103°F. He had conjunctival pallor. JVP was normal. There was no lymphadenopathy. Pulse was 120 per minute and regular. BP was recorded at 145/85 mmHg. Chest examination revealed bronchial breathing on the left side of chest. Cardiovascular and abdominal examinations were normal. Neurological examination revealed no abnormality except absent ankle jerks.

INVESTIGATIONS

Laboratory investigations revealed:

Hb:	8.9 g/dl (normocytic normochromic)	ESR:	105 mm in 1st hour
WCC:	$9.7 \times 10^9/l$	Sodium:	136 mmol/l
	P: 90%, L: 5%,	Potassium:	4.6 mmol/l
		Bicarbonate:	25 mmol/l

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M: 3%, E: 2%	Chloride:	99 mmol/l
Few polymorphs showed toxic granulation	Urine:	normal except mild proteinuria
Platelets: $320 \times 10^9/l$		

QUESTIONS

- Q.1. What is the likely diagnosis?
- Q.2. What other initial laboratory investigations will you order?
- Q.3. What radiological investigations will you order initially?
- Q.4. Name two major complications during the course of disease.
- Q.5. Name a few special laboratory investigations.
- Q.6. Name three drugs commonly used in the treatment.

ANSWERS

- A.1.** In this patient who is anaemic, complaining of fever which is probably due to pneumonia along with aches and pains in his body strongly suggests the diagnosis of multiple myeloma.
- A.2.**
- i. Blood urea and creatinine
 - ii. Serum calcium level
 - iii. Total proteins, albumin, globulins
- All these laboratory investigations are necessary because patients with multiple myeloma may present with renal failure due to presence of light chains in the urine. Increased osteoclastic activity causes hypercalcaemia. The high total protein level with a low albumin indicates increase in monoclonal proteins.
- A.3.**
- i. *Chest X-ray*: There may be evidence of pneumonia.
 - ii. *X-ray lumbo-sacral spine*: Back pain with radiation to both thighs is a common complaint usually due to vertebral collapse.
 - iii. Skeletal survey to see lytic lesions.
 - iv. Abdominal ultrasound to see the size of kidneys. They are generally of normal size but may be enlarged if amyloidosis is present.
 - v. Radio-isotope bone scan is not very helpful as technetium-99m (^{99m}Tc) only picks up osteoblastic activity. It will be positive only if there is a pathological fracture.
- A.4.**
- i. Systemic infections, especially gram-negative septicemia when incidence is higher in the first three months of the diagnosis.
 - ii. Renal failure due to proteinuria and amyloidosis. The precipitation of κ or light chains in renal tubules cause renal failure. These are called Bence Jones proteins (BJP) and 80 percent of the patients show this protein in the urine.
- A.5.**
- i. *Serum protein electrophoresis*: To know monoclonal band of protein. Polyclonal band practically rules out diagnosis of multiple myeloma.

- ii. *Bone marrow examination*: This confirms the diagnosis. A minimum of 15 to 20 percent plasma cells are needed along with other investigations.
- A.6.
- i. Melphalan
 - ii. Cyclophosphamide
 - iii. Corticosteroids.
- NB:** Other new horizons in the treatment of multiple myeloma includes interferon alpha, biphosphonates (pamidronate) as inhibitors of bone resorption, erythropoietin (for treatment of anaemia) and future approaches include interleukin-2, interleukin-4, interferon gamma and tretinoin.

Chronic Myeloid Leukaemia

BRIEF HISTORY

A 68-year-old woman was admitted with a history of increasing shortness of breath, tiredness and poor appetite for the last four months. She had also lost about 5 kg in weight during this period. Her previous medical illness included a fall with Colles fracture two years ago, osteoarthritis and parkinsonism for which she was taking regular paracetamol and L-dopa for the last one year respectively. Six months ago she had urinary tract infection which settled with trimethoprim. She also mentioned that for the last two weeks, she was getting bruises on her skin.

IMPORTANT CLUES ON CLINICAL EXAMINATION

On examination, she was dyspnoeic and moderately anaemic. Blood pressure was 170/90 mmHg. Pulse was 110 per minute and regular. JVP was not raised, clubbing was absent with no thyroid enlargement. There was no palmar erythema or spider naevi. Lymph nodes were not palpable. Heart was in sinus rhythm with a soft systolic apical murmur. Respiratory system was normal. Liver was 3 cm enlarged, firm, smooth and non-tender with no bruit. The spleen was 15 cm enlarged. There was no ascites. Neurological examination was essentially normal.

INVESTIGATIONS

Her initial blood tests were reported as follows:

Hb:	8.6 g/dl	Potassium :	3.3 mmol/l
	(normocytic	Bicarbonate:	25 mmol/l
	normochromic)	Chloride:	97 mmol/l

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WCC:	$89 \times 10^9/l$	Blood urea:	6.8 mmol/l (41 mg/l)
	P:60% L:3%	Creatinine:	136 μ mol/l (1.5 mg/dl)
	M:3% E:2%	Bilirubin:	13 μ mol/l (0.8 mg/dl)
	metamyelocytes:17%	Uric acid:	0.6 mmol/l (10 mg/dl)
	myelocytes: 13%,		
	blast cells:2%		
Platelets:	$300 \times 10^9/l$		
ESR:	53 mm in 1st hour		
Sodium:	143 mmol/l		

QUESTIONS

- Q.1. What is the most likely diagnosis?
- Q.2. Discuss the differential diagnosis.
- Q.3. What four further investigations can help the diagnosis?
- Q.4. What is the role of splenectomy in this condition?
- Q.5. What is the prognosis of this disease in the elderly?

ANSWERS

- A.1.** The most likely diagnosis in this patient along with anaemia, high WCC and increased meta-myelocytes and myelocytes, massive splenomegaly and mildly enlarged liver along with high WCC and increased meta and myeloid series, is chronic myeloid leukaemia (CML).
- A.2.**
- i. Leukemoid reaction which is associated with infections and neoplasms, but the LAP is raised and Philadelphia chromosome is negative.
 - ii. Myelofibrosis in which there is huge splenomegaly, but the LAP is raised and Philadelphia chromosome is absent.
- A.3.**
- i. *Serum B₁₂ levels* There is marked increase in serum levels of B₁₂ due to excessive serum content of transcobalamin I, which is a B₁₂ transport protein.
 - ii. Bone marrow aspiration and biopsy.
 - iii. *Philadelphia chromosome* This is present in 90 percent of cases and consists of shortening of the long arm of chromosome G22 due to translocation of genetic material to chromosome 9. It is unaffected by therapy. Chronic myeloid leukaemia with negative Philadelphia chromosome carries a worse prognosis.
 - iv. *Leukocyte alkaline phosphatase (LAP)* This enzyme is reduced in CML. It is increased in polycythaemia and myelofibrosis. It is low or absent in paroxysmal nocturnal haemoglobinuria (PNH).
- A.4.** Splenectomy is not indicated in patients with chronic myeloid leukaemia. Only rare patients with constant dragging pain due to massive splenomegaly or evidence of hypersplenism may benefit from it.
- A.5.** The median survival time is 2 to 3 years in the elderly. This time is a year or two less than the younger adults.

*Addison's Disease***BRIEF HISTORY**

A female of 38 presented with a four-month history of increasing weakness, tiredness and fatigue. Her appetite had not been so good lately and she had lost 5 kg in weight over the last four months. Her bowel habits had remained normal and there were no urinary symptoms either. She denied having any cough, expectoration, dyspepsia, chest pain, palpitation, headaches or blurring of vision. She was married and had two young children.

IMPORTANT CLUES ON CLINICAL EXAMINATION

On examination, she had an aesthenic build. Blood pressure was 110/60 mmHg. Pulse was 80 per minute and regular. She appeared to be pale, but there was no jaundice, cyanosis, clubbing or oedema. JVP was normal and all the peripheral pulses were palpable. There was some dark brown discolouration of the mucus surface of her lips and buccal mucosa. Teeth and gums were normal. Examinations of respiratory, cardiovascular system, abdomen and central nervous system were normal.

INVESTIGATIONS

Following were the results of various investigations:

Hb:	11.6 g/dl (normocytic normochromic)	Chloride:	99 mmol/l
		Blood sugar:	4 mmol/l (72 mg/dl)
		Blood urea:	8.2 mmol/l (49.2 mg/dl)
WCC:	$8 \times 10^9/l$ P:76% L:20% M:2% E:2%	Creatinine:	103 μ mol/l (1.2 mg/dl)
		Urine:	normal
		ECG:	normal
Platelets :	$258 \times 10^9/l$	Chest X-ray:	small cardiac shadow,
ESR:	27 mm in 1st hour		nil else to note

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Sodium: 132 mmol/l

Potassium : 5.1 mmol/l

Bicarbonate: 24 mmol/l

QUESTIONS

- Q.1. What is the most likely diagnosis?
- Q.2. Give four other causes of buccal pigmentation.
- Q.3. What five further investigations will help your diagnosis?
- Q.4. Give four important causes of this condition.
- Q.5. What is Nelson's syndrome?

ANSWERS

- A.1.** The most likely diagnosis in this 38-year-old woman with weakness, tiredness, fatigue, weight loss, aesthenic build, low blood pressure, pallor, buccal pigmentation, low serum sodium and high potassium is Addison's disease.
- A.2.**
- i. Peutz-Jeghers syndrome.
 - ii. Arsenic, bismuth or silver salts.
 - iii. Metastatic malignant melanoma.
 - iv. Use of anthracin purgatives.
- A.3.**
- i. Plain X-ray abdomen to see adrenal calcification.
 - ii. Serum and urinary cortisol levels.
 - iii. Adrenal auto-antibodies.
 - iv. Synacthen test.
 - v. Mantoux test.
- A.4.**
- i. Autoimmune disorders (80%).
 - ii. Infections (tuberculosis and fungal) not very common now-a-days (15%).
 - iii. Infiltrations (metastases, amyloidosis, etc.) (5%).
 - iv. Acute adrenal haemorrhage (Waterhouse-Friderichsen syndrome which is associated with meningococcaemia).
- A.5.** It is characterised by pigmentation which results due to increased levels of ACTH after bilateral adrenalectomy as treatment of Cushing's syndrome. Later on, this results in chromophobe adenoma of pituitary gland and its complications.

Hyperparathyroidism

BRIEF HISTORY

A 50-year-old lady was admitted with three-month history of bone pains, loss of appetite, constipation and occasional vomiting. She also complained of easy fatigueability, frequency of micturition and recent pain in her left knee. She denied any history of abdominal pain or haematemesis. Due to poor appetite, she had lost about 4 kg in weight over the last two months. She also gave history of passing stones in her urine once or twice. She was taking painkillers and antacids occasionally.

IMPORTANT CLUES ON CLINICAL EXAMINATION

On examination, she looked rather depressed and apathetic but not confused. Her blood pressure was 160/90 mmHg. Pulse was 74 per minute and regular. JVP was not raised. Thyroid and lymph nodes were not palpable. There was no clubbing or obvious bony deformity but movements of the left knee were somewhat painful and limited with moderate joint effusion. Examinations of the abdomen, respiratory and cardiovascular systems were normal. She had loss of sensation of vibration in both legs, but tone and reflexes were normal.

INVESTIGATIONS

The following were the results of various investigations:

Hb:	12 g/dl	Blood urea:	4 mmol/l (24 mg/dl)
	(normocytic	Creatinine:	87 μ mol/l (1.0 mg/dl)
	normochromic)	Serum calcium:	3 mmol/l (12 mg/dl)

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WCC:	8.3 × 10 ⁹ /l	Phosphorus:	0.6 mmol/l (2 mg/dl)
	P:80% L:18%	Serum uric acid:	40 mmol/l (6.2 mg/dl)
	M:1% E:1%	Alk.phos:	456 U/l
Platelets:	260 × 10 ⁹ /l	Urine:	normal
ESR:	13 mm in 1st hour	ECG:	sinus rhythm, no evidence of ischaemia
Sodium:	140 mmol/l	Chest X-ray:	normal
Potassium:	4.2 mmol/l	X-ray left knee:	osteoarthritic changes with a white linear band in the joint cavity.
Bicarbonate:	26 mmol/l		
Chloride:	89 mmol/l		
Blood sugar:	5 mmol/l		
	(90 mg/dl)		

QUESTIONS

- Q.1.** What is the most likely diagnosis?
- Q.2.** What three other investigations will help this diagnosis?
- Q.3.** Give six other causes of hypercalcaemia.
- Q.4.** What is that white linear band in the joint cavity?
- Q.5.** How would you confirm it?
- Q.6.** What treatment can be offered?

ANSWERS

- A.1.** The finding of hypercalcaemia is obvious from the high serum calcium level and its effects, e.g. anorexia, vomiting easy fatigueability, polyuria and general ill health. Hypercalcaemia with low serum phosphorus and high serum alkaline phosphatase, bone pains and X-ray findings of the knee joint favour the diagnosis of primary hyperparathyroidism.
- A.2.**
- i. Estimation of urinary calcium over 24 hours: raised (normal < 150 mg/24 hr.)
 - ii. Prednisolone suppression test: Serum calcium is not suppressed if due to primary hyperparathyroidism.
 - iii. Radioimmunoassay for parathormone.
- A.3.**
- i. Malignancy with bony metastases.
 - ii. Multiple myeloma.
 - iii. Vitamin D excess.
 - iv. Thyrotoxicosis.
 - v. Paget's disease of bone.
 - vi. Sarcoidosis.
- A.4.** This is a classical description of chondrocalcinosis also called pseudo-gout.
- A.5.** Aspiration of synovial fluid from the joint and examining under the microscope would show positively birefringent crystals of calcium pyrophosphates.
- A.6.** It may be divided into medical and surgical treatment:
- Medical treatment* The medical treatment consists of rehydration, drugs such as calcitonin and mithramycin, can be used cautiously. Intravenous phosphate is effective in lowering calcium but can result in widespread metastatic calcification in soft tissues.
- Surgical treatment* The surgical treatment consists of removal of parathyroid glands but replacement therapy with calcium and magnesium should be considered.

Diabetic Retinopathy

BRIEF HISTORY

A fifty eight-year-old man was admitted with one day history of mild left hemiparesis. He had no history of such weakness before. On examination his blood pressure was 150/90 and his pulse was eighty-two per minute regular. There were no significant abnormalities on examination apart from the signs of hemiparesis affecting his left side. He received some physiotherapy and recovered with mild residual weakness but was independent enough to be discharged to his own home. His blood counts and urine examination was normal.

IMPORTANT CLUES ON CLINICAL EXAMINATION

A day before discharge he mentioned about his failing vision which he thought had been gradually coming on for over last three months. He was referred to the ophthalmology department for his eye trouble. When seen in the eye department he was noted to be walking with a stick, but there was no evidence of visual field defect. Intra-ocular pressure, light and accommodation reflexes and eye movements were noted to be normal on both sides. After dilatation of pupil, a small lenticular opacity was noticed in the left eye. Discs were normal too but there were hard exudates on the temporal side with formation of microaneurysms in both eyes. He could count the fingers with both eyes tested separately.

INVESTIGATIONS

Following were the results of various investigations:

Hb:	13.4 g/dl	Bicarbonate:	26 mmol/l
	(normocytic	Chloride:	100 mmol/l
	normochromic)	Blood sugar:	10 mmol/l (180 mg/dl)

Contd...

Contd...

WCC:	9 × 10 ⁹ /l	Blood urea:	9.5 mmol/l (57 mg/dl)
	P:64% L:31%	Creatinine:	138 umol/l (1.5 mg/dl)
	M:3% E:2%	Urine:	protein++, sugar+
Platelets:	250 × 10 ⁹ /l	ECG:	sinus rhythm, T wave
ESR:	22 mm in 1st hour		inversion in left chest
Sodium:	139 mmol/l		leads from V ₃ -V ₆
Potassium:	4 mmol/l	Chest X-ray:	normal

QUESTIONS

- Q.1.** What is the cause for this man's failing vision in the left eye?
- Q.2.** Give a brief account of this cause.
- Q.3.** How do you explain the absence of glycosuria in the urine on his recent admission?
- Q.4.** What is the treatment of his failing vision?
- Q.5.** Give four important causes of gradual loss of vision.

ANSWERS

- A.1.** Probably, diabetic retinopathy and lenticular opacity of his left eye which indicates formation of cataract.
- A.2.** This can be divided into two groups:
- i. *Proliferative*: With soft and hard exudates and haemorrhages along with new vessel formation.
 - ii. *Background*: With microaneurysms.
- A.3.** Because of the increased renal threshold, the diagnosis of diabetes may be missed in up to fifty per cent of the elderly diabetics on simple routine urine examination. A random blood sugar, therefore, is much more appropriate in the elderly subjects. If fasting blood sugar is 150 mg/dl, then diabetes is almost confirmed. If it is between 150 mg/dl and 200 mg/dl, then a glucose tolerance test (GTT) is indicated.
- A.4.**
- i. Adequate control of his diabetes to halt the further progression of retinopathy.
 - ii. Cataract extraction—to improve the vision.
 - iii. Laser treatment for his retinopathy which is either a xenon or argon laser. The later is now-a-days used more commonly.
- A.5.**
- i. Senile cataract (age-related cataract).
 - ii. Chronic glaucoma.
 - iii. Senile macular degeneration (age-related macular degeneration).
 - iv. Retinopathy (diabetic/hypertensive).

Turner's Syndrome

BRIEF HISTORY

A 16-year-old girl was brought by her mother to the gynaecology outpatient department with a history of slow growth since childhood and absence of menstruation. She was also reported to be slow in mentation and had also become hard of hearing. There was no such family history and her brothers and sisters were normal. Nothing else of significance could be found in the past medical history.

IMPORTANT CLUES ON CLINICAL EXAMINATION

On examination, she was short statured with webbing of the neck. Her chest was flat with markedly underdeveloped breasts and widely spaced nipples. She had no anaemia cyanosis or jaundice. Her hands and feet were swollen. Pulse was 88 per minute and regular and BP was 115/75 mmHg. Heart sounds were normal and chest was clear. Abdominal and neurological examinations were unremarkable.

INVESTIGATIONS

Investigations included:

Hb:	11.5 g/dl (normocytic normochromic)	Bicarbonate:	24 mmol/l
		Chloride:	102 mmol/l
WCC:	$6.8 \times 10^9/l$ P:73% L:23% M:2% E:2%	Blood urea:	5.0 mmol/l (30 mg/dl)
		Blood sugar:	6.0 mmol/l (108 mg/dl)
		Creatinine:	119 μ mol/l (1.3 mg/dl)
Platelets:	$240 \times 10^9/l$	Urine:	normal
ESR:	12 mm in 1st hour	ECG:	normal
Sodium:	136 mmol/l	Chest X-ray:	normal
Potassium:	3.4 mmol/l		

QUESTIONS

- Q.1.** What is the most likely diagnosis?
- Q.2.** What further laboratory investigations may help to confirm the diagnosis?
- Q.3.** What other somatic anomalies are associated with this disorder?
- Q.4.** What is the differential diagnosis?
- Q.5.** Can you offer any treatment?

ANSWERS

- A.1.** In this patient with primary amenorrhoea, short stature, webbing of the neck and a flat chest like a shield, the most likely diagnosis is gonadal agenesis of the female (Turner's syndrome).
- A.2.**
- Serum FSH level which is quite high.
 - Serum LH level which is also raised.
 - Serum oestradiol level which is low.
 - Chromosomal analysis: Most individuals are sex chromatin negative and karyotype is 45X. Forty percent are mosaics i.e. 45X/46XX is the most common pattern.
- A.3.** These are mainly the tissues of mesodermal origin and include:
- Low hair line.
 - Redundant skin folds on the back of neck.
 - Micrognathia.
 - Epicanthal folds.
 - Low set or deformed ears.
 - Fish-like mouth.
 - Ptosis.
 - Short fourth metacarpal.
 - Coarctation of aorta.
- A.4.** This condition should be distinguished from:
- Mixed gonadal dysgenesis in which a unilateral testis and a contralateral streak gonad ovary are present.
 - Pure gonadal dysgenesis in which bilateral streak gonads are associated with normal stature and primary amenorrhoea.
 - Noonan's syndrome—which is inherited as autosomal dominant affecting both males and females have normal karyotype and normal gonad; and is also characterised by the presence of webbed neck, short stature, congenital heart disease, cubitus valgus and other congenital defects.
- A.5.** All patients are phenotypically females and at the time of puberty replacement therapy with oestrogen should be instituted to induce maturation of breast, labia, vagina, uterus and fallopian tubes.

Oestradiol treatment if instituted earlier, the predicted height of the patients may be approached. Treatment with growth hormone has not been helpful. To avoid gonadal tumours (malignancies) in patients with mosaics involving chromosome, the gonads should be removed in any patient with evidence of virilization.

Acromegaly

BRIEF HISTORY

A 45-year-old man attended the outpatient department with history of increasing headaches and pain in the knee joints. He also noticed that his shoe size is changing quite rapidly and his finger rings were becoming tight. He had some difficulty in chewing food and used to get tired quickly. His friends noticed that his voice was deep and heavy and sometimes husky. The patient also noticed excessive sweating and small papillomatous lesions over his trunk. At nights he had some tingling sensations in both forearms. Recently, he was getting breathless and was passing excessive amount of urine.

He had no serious illnesses in the past and was not allergic to any drugs. He smoked 20 cigarettes a day.

IMPORTANT CLUES ON CLINICAL EXAMINATION

On examination, he was of large built. His facial features were a bit coarse and he had frontal bossing. There was no pallor, cyanosis, jaundice or clubbing, but his hands were abnormally broad with coarse skin. His pulse was 78 per minute regular and BP was 160/100 mmHg. Cardiovascular system revealed displaced apex beat. Chest was clear. Abdominal examination was unremarkable. Neurological examination revealed bitemporal hemianopia. Fundoscopy was normal.

INVESTIGATIONS

Following investigations were carried out:

Hb :	15.5 g/dl (normocytic normochromic)	Blood urea:	6 mmol/l (36 mg/dl)
		Blood sugar:	10 mmol/l (180 mg/dl)
		Creatinine:	98 umol/l (1.1 mg/dl)

Contd...

Contd...

WCC:	8.4 × 10 ⁹ /l	Urine:	sugar++
	P:72% L:23%	ECG:	sinus rhythm, left ventricular hypertrophy with strain
	M:2% E:3%		
Platelets :	250 × 10 ⁹ /l		
ESR:	14 mm in 1st hour	Chest X-ray:	cardiomegaly, lung fields clear
Sodium:	144 mmol/l		
Potassium :	4.5 mmol/l		
Bicarbonate:	24 mmol/l		
Chloride:	104 mmol/l		

QUESTIONS

- Q.1. What is the diagnosis?
- Q.2. What three investigations would you ask to confirm the diagnosis?
- Q.3. What is the differential diagnosis?
- Q.4. Name a few clinical manifestations of this disease.
- Q.5. Why had the patient developed numbness in the forearms during night?
- Q.6. What treatment can be offered?

ANSWERS

- A.1.** In this patient with a history of headache, coarse features, i.e., broad nose, frontal bossing and rapidly changing size of shoes with clinical evidence of cardiomegaly, hypertension, bitemporal hemianopia and biochemically hyperglycaemia and glycosuria point to a diagnosis of acromegaly.
- A.2.** These include:
- i. X-ray skull—lateral view to measure the dimensions of pituitary fossa. The pituitary fossa is enlarged, may have double floor and erosions of clinoid processes. (CT scan is useful to know the extension to the surrounding structure. MRI even gives better definitions of tumour).
 - ii. Non-suppression of growth hormone (GH) with a glucose tolerance test. Normally, the growth hormone is suppressed with glucose load but in acromegalics it may paradoxically rise.
 - iii. Growth Hormone (GH) assay: It is always elevated and gives an abnormal release response to TRH. IGF (intermediate growth factor-I). Somatomedin-C reflects mean 24 hour growth hormone levels and is useful in diagnosis.
- A.3.** The only differential diagnosis is Toraine-Solanti-Gole syndrome in which features are like acromegaly but growth hormone is normal.
- A.4.**
- i. Excessive perspiration
 - ii. Hypertrichosis
 - iii. Acanthosis nigricans
 - iv. Fibromata mollusca
 - v. Chondrocalcinosis
 - vi. Hypercalcaemia
- A.5.** This was due to median nerve trapement at wrist, as carpal tunnel syndrome is quite common in acormegaly.
- A.6.** There are several methods:
- i. Transfrontal and trans-sphenoidal approaches are used for microsurgery in removing adenomas.
 - ii. Irradiation, both proton beam or heavy particle

treatment can reduce growth hormone level in 80 percent of patients but takes 1 to 10+ years to be effective.

- iii. Several medical treatments have been tried but failed. Somatostatin (octreotide) in 50 to 100 micrograms lowers the GH level but is given in the form of continuous infusion. Bromocriptine in heavy doses also shrinks the tumour.

In some cases, combination of all these three modes of treatment is necessary.

Klinefelter's Syndrome

BRIEF HISTORY

A 19-year-old man presented to the medical outpatient department complaining that his breasts were enlarged. He had noticed gradual increase in their size in the last one year. He felt embarrassed and wanted immediate remedy. He denied any pain in the breast. He had also noticed that his frequency of shaving was less frequent than others. He denied any hospitalization or any history of hypertension or diabetes. He was a graduate in the university and denied smoking or taking any drugs or alcohol.

IMPORTANT CLUES ON CLINICAL EXAMINATION

On examination, he had a fair complexion and was quite tall. He had a pulse of 78 per minute regular and BP of 115/80 mmHg. Cardiovascular, respiratory, abdominal and neurological examinations were normal. He had small genitalia.

INVESTIGATIONS

The following investigations were asked.

Hb:	12.5 g/dl	Bicarbonate:	24 mmol/l
	(normocytic	Chloride:	102 mmol/l
	normochromic)	Blood urea:	4 mmol/l (24 mg/dl)
WCC:	$8 \times 10^9/l$	Blood sugar:	5 mmol/l (90 mg/dl)
	P:70% L:28%	Creatinine:	87 $\mu\text{mol/l}$ (0.9 mg/dl)
	M:1% E:1%	Urine:	normal
Platelets:	$310 \times 10^9/l$	ECG:	normal
ESR:	10 mm in 1st hour	Chest X-ray:	normal
Sodium:	136 mmol/l		
Potassium:	3.4 mmol/l		

QUESTIONS

- Q.1.** What is the most likely diagnosis?
- Q.2.** What investigations would you ask for?
- Q.3.** What diseases can be associated with this condition?
- Q.4.** What is the management?

ANSWERS

- A.1.** In a man of 19 who complains of gynaecomastia, decreased frequency of shaving with a tall stature and small genitalia is likely to be Klinefelter's syndrome.
- A.2.**
- i. Plasma levels (elevated) of gonadotropins LH, FSH.
 - ii. Urinary levels (elevated) of gonadotropins LH, FSH and decreased levels of testosterone.
 - iii. Semen analysis—azoospermia.
 - iv. Karyotyping from buccal mucosa. – 47 xxy (Classical) 46xy/47xxy (Mosaic).
 - v. Testicular biopsy—hyalinization of the tubules, absence of spermatogenesis and apparent increase in Leydig's cells.
- A.3.**
- i. Diabetes mellitus.
 - ii. Pulmonary disease.
 - iii. Thyroid dysfunction/subnormality.
 - v. Sterility.
- A.4.** No method can reverse the sterility. If gynaecomastia is troublesome, only the surgical treatment may be beneficial. Some patients may benefit from supplements of androgens, but it can paradoxically worsen the gynaecomastia, presumably by providing increased substrate androgen for conversion to oestrogen.

Conn's Syndrome

BRIEF HISTORY

A 39-year-old woman presented with increasing headache and breathlessness on exertion for about four months. She consulted a few general practitioners who diagnosed hypertension and treated with some medications which she did not remember, but her blood pressure never became normal. She also told about increased fatigue and weakness. On two occasions she had fluttering in her chest but no chest pain. There was no previous history of any serious illnesses and she admitted that recently she was passing excessive quantities of urine and was feeling thirsty most of the time. No allergies were noticed.

IMPORTANT CLUES ON CLINICAL EXAMINATION

On examination, she was medium built, rather anxious. There was no pallor, cyanosis, jaundice, clubbing or lymphadenopathy. She had no poedal oedema. Her pulse was 78 per minute and blood pressure was 150/115 mmHg. Heart sounds were normal. Chest revealed a few bibasal crackles. Abdomen was soft, non-tender with no visceromegaly. Neurologically there were no signs and fundi showed, a few exudates but no haemorrhages or papilloedema.

INVESTIGATIONS

Following investigations were asked:

Hb :	14.5 g/dl	Bicarbonate:	28 mmol/l
	(normocytic	Chloride:	110 mmol/l
	normochromic)	Blood urea:	8 mmol/l (48 mg/dl)

Contd...

Contd...

WCC:	7.9 × 10 ⁹ /l	Creatinine:	110 µmol/l (1.2 mg/dl)
	P:72% L:26%	Blood sugar:	5.6 mmol/l (100 mg/dl)
	M:1% E:1%	Urine:	normal
Platelets:	310 × 10 ⁹ /l		
ESR:	34 mm in 1st hour		
Sodium:	150 mmol/l		
Potassium:	2.8 mmol/l		

QUESTIONS

- Q.1. What is the most likely diagnosis?
- Q.2. What further investigations would be helpful?
- Q.3. Give differential diagnosis.
- Q.4. What is the cause of your diagnosis?
- Q.5. What treatment could be offered?
- Q.6. What are the side effects of the 'drug' used for this condition?

ANSWERS

- A.1.** In a female patient, who presents with headache and high blood pressure clinically with no evidence of failure, i.e. oedema, and biochemically high sodium and low potassium goes in favour of hyperaldosteronism—Conn's syndrome.
- A.2.**
- i. Chest X-ray—to show left ventricular enlargement.
 - ii. ECG—to show left ventricular hypertrophy and strain—also signs of potassium depletion, i.e. U wave and premature contractions.
 - iii. Low plasma renin activity which fails to increase appropriately during volume depletion.
 - iv. Hypersecretion of aldosterone which fails to suppress during volume expansion.
 - v. CT scan—of both adrenals.
- A.3.**
- i. Accelerated hypertension—renin is high while in Conn's it is low.
 - ii. Hyper mineralocorticoid state.
 - iii. Liquorice ingestion—diagnosis excluded by careful history.
- A.4.** Either it may be due to hyperplasia or adenoma of the mineralocorticoid producing (zona glomerulosa) part of adrenal cortex. It may be unilateral or bilateral.
- A.5.** If it is due to adenoma, then surgical excision is required. Dietary restriction of sodium and potassium supplements are important. Spironolactone, which is aldosterone antagonist is also useful, 25 mg to 100 mg of spironolactone (Aldactone) after every eight hours, usually controls hypernatraemia and hypokalaemia.
- A.6.** These are common in males, i.e.
- i. Gynaecomastia
 - ii. Decreased libido
 - iii. Impotence.

Hypothyroidism

BRIEF HISTORY

A 58-year-old lady attended the medical outpatient department with four months history of deafness, poor mobility and occasional falls. Her daughter told that her mother was getting sluggish and very slow to respond. Her appetite had remained unchanged and it was noticed by her daughter that mother was putting on weight and she was most of the time sleeping. The patient revealed that she was more constipated and she used to get tired while speaking. There was no history of cough, expectoration, chest pain, palpitation or urinary symptoms.

IMPORTANT CLUES ON CLINICAL EXAMINATION

On examination, she was obese, pale and mildly confused. Her voice was gruffy and rather hoarse. She had scarce hair on her scalp and puffiness of her both lower eyelids. Hair distribution was normal, but her skin was somewhat dry and thickened. Her pulse was 62 per minute and regular. Blood pressure was 150/90 mmHg lying, 140/78 mmHg standing. There was no thyroid or lymph node enlargement. Apex beat was not easily palpable, but she was in sinus rhythm with no murmur. Respiratory system and abdominal examinations were normal. She had sluggish tendon reflexes and loss of sense of vibration, but otherwise the neurological examination was unremarkable. On simple mental function testing she scored 6 out of 10.

INVESTIGATIONS

Following were the results of various investigations:

Hb :	10.9 g/dl (macrocytic normochromic)	Bicarbonate:	24 mmol/l
		Chloride:	102 mmol/l
WBC:	$7.4 \times 10^9/l$ P:78% L:19% M:2% E:1%	Blood urea:	10.8 mmol/l (64.8 mg/l)
		Creatinine:	138 μ mol/l (1.5 mg/dl)
MCV:	95fl	Blood sugar:	7.1 mmol/l (128 mg/dl)
ESR:	38 mm in 1st hour	Urine:	protein+, sugar, nil, bacteria+++.
Sodium:	134 mmol/l	ECG:	normal sinus rhythm
Potassium:	4 mmol/l		

QUESTIONS

- Q.1.** What is the most likely diagnosis?
- Q.2.** What are the neuropsychiatric features of this disease?
- Q.3.** What two investigations will confirm your diagnosis in this patient?
- Q.4.** How would you treat this patient?

ANSWERS

A.1. The most likely diagnosis in this lady with a non-specific picture of declining mobility and general health, deafness, few falls, slowness and weight gain, mild confusion, puffiness of eyelids and dry skin is hypothyroidism. Hypothyroidism can present with a typical feature and the diagnosis is usually made clinically and confirmed biochemically. In addition to myxoedema, this lady has urinary tract infection.

- A.2.** i. *Neurological:*
- a. Neuropathy e.g. hearing loss
 - b. Carpel tunnel syndrome or entrapment neuropathy.
 - c. Cerebellar syndrome
- ii. *Psychiatric:*
- a. Hallucination
 - b. Paranoid ideas
 - c. Depression, attempted suicide is possible.
 - d. Dementia (myxoedema madness)

- A.3.** i. Serum T_3 T_4 usually low.
- ii. TSH level—very high in primary hypothyroidism, but in secondary type all values are low.

NB: Hypothyroidism is diagnosed when there is dry rough skin, slow mentation etc. but if there is gross puffiness of the tissues due to myxomatous deposition, then it is called myxoedema. Both are confirmed by thyroid function tests. Hypothyroid patients may not be myxoedematous but myxoedematous patients are almost always hypothyroid.

- A.4.** The treatment is with thyroxine. To start with low dose of thyroxine, i.e. 25 micrograms per day and gradually increased to 50, then 100 micrograms after 4 to 6 week intervals until the dose becomes 200 to 300 micrograms daily and the patient feels better. If the patient is a young hypothyroid, then one can start with higher dose and then taper to the most suitable dose to control the symptoms. One should monitor the response by ECG recording once a week to see any ST-T changes.

Cushing's Syndrome

BRIEF HISTORY

A 36-year-old housewife presented with a three-month history of excessive weight gain, facial hair growth and weakness. She had gained about 4 kg of weight during the last three-months. Her diet and level of physical activities had not changed significantly. She had found the facial hair growth embarrassing, and in spite of the fact that she had shaved frequently, she had not felt like going out in recent weeks. She felt depressed and weak and also noticed that she was developing bruises on the skin easily. There was no history of urinary symptoms and her bowels were normal. She lived with her husband and three young children. Her periods were regular and she was not taking any drugs including contraceptive pills. There was no significant history of past illness.

IMPORTANT CLUES ON CLINICAL EXAMINATION

On examination, she was obese, weight was 71 kg, height was 5 ft 1 inch. JVP was normal. Blood pressure was 160/100 mmHg. Pulse was 78 per minute and regular. Peripheral pulses were normal. There was no anaemia, cyanosis, jaundice, clubbing or oedema. She had a few hair on her chin and above upper lip. Abdomen was distended with stretch marks on the skin. Respiratory and neurological examinations were normal. She was not pregnant.

INVESTIGATIONS

Results of the following investigations were available:

Hb :	13.8 g/dl	Bicarbonate:	24 mmol/l
	(normocytic	Chloride:	102 mmol/l
	normochromic)	Blood urea:	5.0 mmol/l (30 mg/dl)

Contd...

Contd...

WCC:	6.8 × 10 ⁹ /l	Creatinine:	80 umol/l (0.9 mg/dl)
	P:70% L:26%	Blood sugar:	7.0 mmol/l(126 mg/dl)
	M:2% E:3%	Urine:	normal
Platelets:	300 × 10 ⁹ /l	ECG:	normal sinus rhythm
ESR:	22 mm in 1st hour		In history the pulse is
Sodium:	140 mmol/l		regular.
Potassium:	2.4 mmol/l		

QUESTIONS

- Q.1. What is the most likely diagnosis?
- Q.2. What are the causes of this diagnosis?
- Q.3. What further five investigations will help your diagnosis?
- Q.4. Describe an importantly related test and its significance which differentiates the origin of this disease.
- Q.5. What name is given to the condition after surgical management of this disease?

ANSWERS

- A.1.** The most likely diagnosis in this lady with truncal obesity, weight gain, excessive hair growth, weakness, mildly raised blood pressure, normal serum sodium and low serum potassium is Cushing's syndrome.
- A.2.**
- Excessive secretion of ACTH by the pituitary gland.
 - Hyperfunction of adrenal cortex (adenoma/carcinoma) due to hyperplasia.
 - Exogenous administration of steroids.
- A.3.**
- Measurement of morning and evening plasma cortisol level. High level of plasma cortisol with loss of diurnal variation will suggest the diagnosis.
 - Measurement of free cortisol in the urine. High urinary output of free cortisol would be expected.
 - Dexamethasone suppression test. *Small dose* test (0.5 mg dexamethasone orally QID for 48 hours). Dexamethasone test is done to establish that the patient is of hypercortisolism (Cushing's syndrome), whereas a *large dose* test (2 mg 6 hourly for 48 hours) is performed to see the control of pituitary on adrenal function. In cases of excessive ACTH secretion from the pituitary (Cushing's disease), the suppression of adrenal function is seen. Patients with adrenal tumour and ectopic production of ACTH do not respond.
 - Chest X-ray and X-ray of the pituitary fossa.
 - Abdominal CT scan to see any adrenal cortical tumour (adenoma/carcinoma).
- A.4.** *Metyrapone test:* This agent inhibits 11-B-hydroxylase and the precursors are raised which are measured as 17-OGS (oxogenic steroids). The procedure includes collection of urine for three days. On the second day Metyrapone is started at 0900 hr as 750 mg 4 hourly for 6 doses. The maximum 17-OGS occur either on the day of administration or day after.
- Normal excretion in 24 hours is 80 to 160 umol. In Cushing's disease, there is exaggerated response. In non-pituitary dependent Cushing's syndrome, no increase in urinary 17-OGS is seen.

It provides satisfactory test in distinguishing the pituitary dependent from the non-pituitary dependent causes of Cushing's syndrome.

- A.5. *Nelson's syndrome:*** This is characterised by hyperpigmentation of the body after bilateral adrenalectomy for Cushing's syndrome and is due to increase in ACTH production and stimulation of melanocytes by the MSH containing polypeptides of ACTH. This may also result in pituitary adenoma (ACTH producing).

Hyperthyroidism

BRIEF HISTORY

A 52-year-old woman was admitted with three-month history of undue tiredness, shortness of breath on exertion, swelling of both legs and occasional palpitations which she described as butterflies in the chest. She denied having any chest pain. Her appetite had been good and she had not lost any weight. Bowels were normal and there were no urinary symptoms. She also complained of rumbling noise in her abdomen and it was told by her daughter that she felt very uncomfortable in hot weather. She also had become a little bit irritable and on times disorientated and rather confused.

IMPORTANT CLUES ON CLINICAL EXAMINATION

On examination, she looked tired and apathetic and was mildly confused. JVP was raised by 2 cm and she had bilateral pitting ankle oedema. Blood pressure was 160/80 mm Hg sitting, 155/90 mm Hg standing. Pulse was 130 per minute and irregular. Her palms were sweaty. Apex beat was in fifth intercostal space inside mid-clavicular line. Thyroid and lymph nodes were enlarged. She had tremours in her both hands when stretched out, but there was no lid lag or exophthalmos. She had bilateral crackles in her chest. Apex rate was 140 irregular and she had a widespread soft systolic murmur. Abdomen was normal and there were no localising neurological signs. She could walk without any help.

INVESTIGATIONS

The following were the results of various investigations:

Hb :	12.4 g/dl (normo-cytic normochromic)	Serum T ₃ :	3.2 ug/l (normal 0.7-2 ug/l)
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Contd...

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WBC:	6.9 × 10 ⁹ /l	Blood urea:	10 mmol/l (60 mg/dl)
	P:82% L:16%	Creatinine:	139 µmol/l (1.6 mg/dl)
	M:2% E:1%	Blood sugar:	6.7 mmol/l (121 mg/dl)
Platelets:	310 × 10 ⁹ /l	Urine:	normal
ESR:	29 mm in 1st hour	ECG:	atrial fibrillation with
Sodium:	136 mmol/l		some ischaemic changes,
Potassium:	4.1 mmol/l		no acute infarction.
Bicarbonate:	27 mmol/l	Chest X-ray:	normal
Chloride:	96 mmol/l		

QUESTIONS

- Q.1.** What is the most likely diagnosis?
- Q.2.** Give five causes of falsely high T₃ results.
- Q.3.** Give five causes of falsely low T₃ results.
- Q.4.** What is Plummer's nail?
- Q.5.** What is the triad associated with this disease?
- Q.6.** Briefly outline the differential diagnosis.

ANSWERS

- A.1.** The most likely diagnosis in this elderly lady with tiredness, dyspnoea, palpitation, occasional confusion, fine tremours, intolerance to heat, raised JVP, oedema, rapid atrial fibrillation and raised serum T_3 , is T_3 thyrotoxicosis. Atypical presentation of thyrotoxicosis is common in the elderly and features, such as diarrhoea, anxiety, weight loss, increased appetite and eye signs, may be completely missing thus rendering the difficulty in the diagnosis.
- A.2.**
- i. Pregnancy
 - ii. Oestrogen therapy
 - iii. Phenothiazine therapy
 - iv. Clofibrate therapy
 - v. Viral hepatitis.
- A.3.**
- i. Nephrotic syndrome
 - ii. Malnutrition
 - iii. Androgen therapy
 - iv. Steroid therapy
 - v. After surgery or prolonged ill health.
- A.4.** This is a type of onycholysis, in which there is a triangular involvement of the edge of the nail with the base facing towards the periphery. Further progression leads to separation of the nail from the nailbed.
- A.5.**
- i. Diffuse goitre
 - ii. Exophthalmos
 - iii. Pre-tibial myxoedema. All of the above form triad of Graves' disease.
- A.6.**
- i. Anxiety
 - ii. Metastatic malignant disease
 - iii. Hypokalaemia.

Pheochromocytoma

BRIEF HISTORY

A 29-year-old woman was admitted in the gynaecology and obstetrics department for the delivery of her first baby. Antenatal record showed that she had high BP and also developed marked oedema of feet. BP recorded was 210/150 mmHg which was checked twice and monitored regularly, but it remained high. At this BP, foetal distress started and she was referred to the medical department for management of her BP. She was started on beta-blockers but unfortunately, it was too late and the foetus died *in utero* and she was delivered by caesarean section. In spite of this, her BP did not settle down and it persisted 190/110 to 200/130 mmHg. She never had such high BP in the past although at times she complained of palpitations, sweating and her relatives telling her that she looked pale. Her menstrual history was unremarkable and she had no family history of hypertension or diabetes. She gave no history of allergies either.

IMPORTANT CLUES ON CLINICAL EXAMINATION

On examination, she was a thin built lady. Pallor was obvious and there was no cyanosis, jaundice, clubbing or lymphadenopathy. Her pulse was 120 per minute and regular and BP was 190/125 mmHg without postural drop. Heart sounds were clearly audible and chest was clear. Abdominal examination revealed low segment caesarean section scar. A round mass was palpable in the right loin but due to recent operation it was very difficult to clearly out line. No neurological deficit was noticed.

Her tongue is shown in Figure 67.1.

INVESTIGATIONS

Investigations which were carried out were as follows:

Hb :	9.8 g/dl (normocytic normochromic)	Chloride:	102 mmol/l
		Blood urea:	6 mmol/l (36 mg/dl)
WBC:	$12.2 \times 10^9/l$ P:76% L:20% M:2% E:2%	Creatinine:	138 $\mu\text{mol/l}$ (1.6 mg/dl)
		Blood sugar:	4.6 mmol/l (83 mg/dl)
Platelets:	$280 \times 10^9/l$	Urine:	traces of proteins, no sugar.
Sodium:	138 mmol/l	ECG:	sinus tachycardia
Potassium:	4.5 mmol/l	Chest X-ray:	normal
Bicarbonate:	25 mmol/l		



Fig. 67.1

QUESTIONS

- Q.1. What is the most likely diagnosis?
- Q.2. What further investigations would you ask for?
- Q.3. Describe another test which can help in the diagnosis.
- Q.4. Is the appearance of tongue in this particular patient of any significance?
- Q.5. How would you treat such patients?

ANSWERS

- A.1.** In a young patient who developed high blood pressure, not controlled by beta blockers, tachycardia, pallor and sweating, *in utero* death of the foetus and a vague mass in the right loin points to a likely diagnosis of pheochromocytoma.
- A.2.**
- i. Twenty-four hours urine analysis for vanillyl mandelic acid (VMA). It should not be more than 8 mg/24 hours.
 - ii. Abdominal ultrasound to see a mass in the suprarenal area.
 - iii. MIBG (^{131}I -meta-iodobenzyl-guanidine) scanning is also helpful as this compound has structural similarities to noradrenaline and is taken up by catecholamine secreting tumours.
 - iv. Selective venous sampling is the most reliable method for localizing the catecholamine secreting tumour.
 - v. CT scanning will outline the tumour itself and surrounding structures.
- A.3.** Pentolinium test: It is a ganglion blocker and reduces the release of catecholamines from pheochromocytoma and suppresses it. There is a significant drop in the level of catecholamines within the first 20 minutes after an injection of 2.5 mg of pentolinium. Whereas in ectopic sources of catecholamines, this is not suppressed.
- A.4.** Yes. The tongue shows mucosal neuromas which is a part of MEN type III syndrome and is associated with sub-ungual angioma and pheochromocytoma.
- A.5.** Pre-operative control of BP is very important and that can be done with both alpha and beta blockers. Phenoxymethamine (alpha blocker) and propranolol (beta blocker) are used in combination. When the BP is controlled, then adrenalectomy is performed. Other medical therapy include labetalol and carvedilol.
- NB:** VMA (vanillyl mandelic acid) may be falsely high in these conditions: Guillain-Barre syndrome, intracranial lesions, convulsions, hypoglycaemia, carcinoid syndrome, acute porphyria, lead poisoning.

Diabetic Amyotrophy

BRIEF HISTORY

A 63-year-old man was admitted in the ward with a history of painful right thigh and increasing difficulty in climbing the stairs for the last four weeks. He also complained off and on cramp like pain in his both calves. He was known late onset diabetic but was well controlled with oral hypoglycaemic agents in the recent past. Recently, he had experienced excessive thirst and passed urine at night more frequently. He had lost 6.5 kg in weight over the last three weeks. He had attended casualty department following a fall while getting out of the bathroom about ten days ago, but he was sent home since there was no evidence of bony injury on the X-ray of his pelvis and hips. He was not known hypertensive. He occasionally smoked five to six cigarettes per day.

IMPORTANT CLUES ON CLINICAL EXAMINATION

On examination, he was mentally alert. There was no clubbing, cyanosis, lymphadenopathy, anaemia or jaundice. Examination of cardiovascular system showed feeble femoral pulses and both dorsalis pedis were hardly palpable. Respiratory system showed bilateal crackles and abdomen was normal. He had hard exudates in his fundi. There was wasting of thigh muscles and they were weak as well without sensory changes. Reflexes were normal apart from sluggish knee jerks on both sides and absent ankle jerks.

INVESTIGATIONS

Following were the various investigations:

Hb :	14 g/dl (normocytic	Bicarbonate:	21 mmol/l
	normochromic)	Chloride:	100 mmol/l

Contd...

Contd...

WBC:	10 × 10 ⁹ /l	Blood urea:	13 mmol/l (78 mg/dl)
	P:79% L:18%	Creatinine:	140 umol/l (1.6 mg/dl)
	M:2% E:1%	Blood sugar:	23 mmol/l (414 mg/dl)
HbA _{1C} :	11g/l (5-8g/dl)	Urine:	sugar+++ , no ketones
Platelets:	300 × 10 ⁹ /l	ECG:	normal sinus rhythm
ESR:	32 mm in 1st hour		with ventricular ectopics.
Sodium:	140 mmol/l	Chest X-ray:	normal
Potassium:	5.2 mmol/l		

QUESTIONS

- Q.1.** What is the most likely diagnosis?
- Q.2.** Give two investigations which will help the diagnosis.
- Q.3.** What is the significance of HbA_{1C} of 11g/dl?
- Q.4.** Give two measures helpful in treating this patient.

ANSWERS

- A.1.** This elderly gentleman with late onset diabetes mellitus and retinopathy, probably, has diabetic amyotrophy as suggested by his proximal muscular weakness and painful thighs, with no sensory deficit. It seems that his diabetes has been out of control recently as is the usual case in most patients with amyotrophy.
- A.2.** i. Electromyography—low and multiphasic potentials.
ii. Muscle biopsy—infiltration of inflammatory cells and fibroblast with atrophy of the muscle fibres.
- A.3.** The level of HbA_{1C} is used as cumulative index of general level of hyperglycaemia in diabetic patients over the past three to six months. If over 12 to 15 percent it represents a poor control of diabetes. It takes a few weeks for HbA_{1C} to fall once the good control has been re-established.
- A.4.** i. Good control of diabetes mellitus.
ii. Physiotherapy.
- NB:** When there is lancinating pain, sensory ataxia with mild weakness along with bowel and bladder derangements, it resembles that of tabes dorsalis so closely that the name diabetic tabes is given.

S-I-A-D-H Syndrome

BRIEF HISTORY

A 57-year-old gentleman was admitted to medical ward via accident and emergency department with a ten-day history of fever, cough, purulent sputum and chest pain. The pain was pleuritic in nature and was more on coughing or taking a deep breath. He was a shopkeeper by profession and had no other symptoms except what the wife told. She told that he had been confused recently and was doing things which he normally never did in the past. He was not a known diabetic or hypertensive, but he smoked twenty-five cigarettes per day.

IMPORTANT CLUES ON CLINICAL EXAMINATION

On examination, he looked toxic and drowsy. Temperature was 103°F and pulse was 110 per minute and regular. His BP was 140/80 mm Hg while lying and 135/80 mm Hg while standing. There was no jaundice, cyanosis, clubbing or lymph node enlargement. Cardiovascular and abdominal examinations were normal. However, he had dullness in his right base and bronchial breathing with a pleural rub on his chest examination. There were a few crackles, too. Neurological examination revealed that he was confused and thought that he was at home. Rest of the neurological examination was normal.

INVESTIGATIONS

Investigations included.

Hb:	13.5 g/dl	Bicarbonate:	25 mmol/l
	(normocytic	Chloride:	96 mmol/l
	normochromic)	Blood urea:	8 mmol/l (48 mg/dl)

Contd...

Contd...

WBC:	17 × 10 ⁹ /l	Creatinine:	130 umol/l (1.5 mg/dl)
	P:80% L:15%	Blood sugar:	6.8 mmol/l (122 mg/dl)
	M:4% E:1%	Urine:	normal
Platelets:	250 × 10 ⁹ /l	ECG:	sinus tachycardia
ESR:	60 mm in 1st hour		
Sodium:	118 mmol/l		
Potassium:	4.2 mmol/l		

QUESTIONS

- Q.1.** What is the most likely diagnosis?
- Q.2.** Why is he confused?
- Q.3.** How do you differentiate this hyponatraemia from that due to Addisons's disease clinically?
- Q.4.** What four investigations would you ask for this patient?
- Q.5.** Name a few drugs which may mimic this condition.
- Q.6.** Mention a few respiratory conditions which may be associated with this.

ANSWERS

- A.1.** In a patient who has been a smoker and now presents with cough, purulent sputum and clinically with signs of consolidation points towards diagnosis of pneumonia. Underlying bronchogenic carcinoma cannot be ruled out.
- A.2.** Investigations show that the sodium level is 118 mmol/l and such a degree of hyponatraemia causes cerebral oedema and confusion. This is due to inappropriate release of antidiuretic hormone.
- A.3.** In this case, there is no postural drop in the BP indicating that intravascular volume is normal, whereas in Addison's disease there is postural drop of BP. The serum K^+ levels are normal, while in Addison's disease it is high.
- A.4.**
- Sputum examination for Gram stain, AAFB and malignant cells.
 - Chest X-ray showing consolidation.
 - Plasma and urinary osmolarity, the former is low and the latter is high.
 - Bronchoscopy may show a bronchogenic carcinoma.
- A.5.**
- Chlorpropamide.
 - Thiazide diuretics.
 - Phenothiazine derivatives.
 - Tricyclic antidepressants/SSRI and NSSRI antidepressants.
- A.6.**
- Pneumonias.
 - Oat cell carcinoma of lung.
 - Positive pressure ventilation (PPV).
 - Pulmonary tuberculosis.

Renal Tubular Acidosis

BRIEF HISTORY

A male child of 12 years presented to the outdoor department by his parents with a history of stunted growth and difficulty in walking. The early milestones were more or less normal, but later on he was noticed to be lacking behind in his studies and also complained of undue lethargy. It was also noticed by the parents, that he was passing more than normal amounts of urine, however, there was no history of anorexia or diarrhoea or steatorrhoea. No other family members had such problems. His parents were not diabetic either.

IMPORTANT CLUES ON CLINICAL EXAMINATION

On examination, his height was short and he looked smaller for his age. He had prominent frontal sinuses and forehead and both of his legs were bent. He looked a bit pale. His pulse was 82 per minute. There was no facial puffiness or oedema. His cardiovascular, respiratory, abdominal and neurological examinations were unremarkable.

INVESTIGATIONS

Following investigations were asked:

Hb :	11.2 g/dl (normocytic normochromic)	Blood Sugar:	5.6 mmol/l (101 mg/dl)
		Blood urea:	5.5 mmol/l (33 mg/dl)
		Creatinine:	106 umol/l (1.2 mg/dl)
WCC:	$8.9 \times 10^9/l$	Arterial blood gases:	
	P: 78% L: 20%	pH:	7.28 and
	M: 2% E: 0%	PCO ₂ :	4.12 kPa (30 mm Hg)

Contd...

Contd...

Platelets:	280 × 10 ⁹ /l	PO ₂ :	11.53 kPa (90 mm Hg)
ESR:	15 mm in 1st hour	HCO ₃ ⁻ :	16 mmol/l
Sodium:	138 mmol/l	Urine:	pH 7.0, pus cells 10-12/ hpf, bacteria++
Potassium:	3 mmol/l	ECG:	normal
Chloride:	112 mmol/l	Chest X-ray:	normal
Calcium:	1.8 mmol/ (7.2 mg/dl)		
Albumin:	4g/dl		

QUESTIONS

- Q.1.** What is the most likely diagnosis?
- Q.2.** What is the differential diagnosis?
- Q.3.** What further investigations can be asked to confirm the diagnosis?
- Q.4.** What treatment can be offered?

ANSWERS

- A.1.** In a child of 12 years who has obvious stunted growth with skeletal deformities along with metabolic acidosis and hypokalaemia, hyperchloraemia and hypocalcaemia in the absence of obvious renal failure and malabsorption, the most likely diagnosis is renal tubular acidosis (RTA) leading to rickets with hyperchloraemic metabolic acidosis.
- A.2.** It should be differentiated from:
- Vitamin D deficiency—rickets
 - Hypophosphataemic rickets—it is X-linked dominant and is resistant to vitamin D.
 - Hypophosphataemia.
 - Fanconi's syndrome—there is generalised amino aciduria, phosphate wasting, metabolic bone disease, renal tubular acidosis type 2 (proximal RTA) and glycosuria.
- A.3.** These investigations include:
- X-ray KUB-and/or ultrasound abdomen to see nephrocalcinosis or nephrolithiasis—in this case if present means classical or type 1 or distal RTA.
 - Urine pH—if urine pH is more than 5.5 despite the presence of metabolic acidosis, it means that renal tubules are unable to acidify the urine.
 - Ammonium chloride (NH_4Cl) loading test—if urine pH falls below 5.4, it means proximal renal tubular acidosis (type 2), but if it remains above 5.4 it means distal renal tubular acidosis (type 1).
 - Urinary calcium—there is hypercalciuria, so it is increased $> 4 \text{ mg/kg/day}$ (normal $100\text{--}300 \text{ mg/24 hour}$).
 - Urinary citrate is low in distal (type 1) and normal in proximal (type 2).
- A.4.** The mainstay of treatment in renal tubular acidosis is the administration of alkali in amounts necessary for correction of metabolic acidosis. The requirement of HCO_3^- is more in type 2 and in children as much as $4 \text{ to } 14 \text{ mmol/kg/day}$. Many patients can be treated only with NaHCO_3 or sodium citrate (Bicitra) since potassium wasting is markedly diminished when acidosis is corrected, particularly, in distal RTA (type 1).
In proximal RTA, alkali therapy may increase potassium wasting, so potassium citrate alone or with sodium citrate (Polycitra) is indicated.

Carcinoma Prostate

BRIEF HISTORY

A 61-year-old man presented to the outpatient department with a history of severe bone pains and aches all over the body, more so in the lower back and left side of the chest. For the last ten days, he had pain in the right loin. For the last three months, he had noticed difficulty in passing urine and had to wake up four to five times during night. Once or twice, he had passed red-coloured urine. There was no history of fever. He felt generalised weakness, malaise and anorexia. One week prior to his present visit, he was brought to the accident and emergency department with acute retention of urine and about 1000 c.c. of urine was drained with a catheter. He was not a known diabetic but suffered from hypertension. He gave up smoking about five years ago. No drug allergies were noticed.

IMPORTANT CLUES ON CLINICAL EXAMINATION

On examination, he looked wasted and pale. There was no lymphadenopathy or jaundice. He was tender in the lower back. BP was 140/85 mmHg. Chest was clear, but he was tender on the left side just below the scapula. Cardiovascular and neurological examinations were unremarkable. There was no visceromegaly, but digital examination of the rectum revealed that prostate was enlarged and rectal mucosa was adherent to it.

INVESTIGATIONS

Investigations included:

Hb:	8.8 g/dl (macro-cytic hypochromic)	Bicarbonate:	25 mmol/l
		Chloride:	99 mmol/l
		Blood urea:	13 mmol/l (78 mg/dl)

Contd...

Contd...

WCC:	10.2 × 10 ⁹ /l	Creatinine:	234 µmol/l (2.7 mg/dl)
	P:72% L:22%	Blood sugar:	5.1 mmol/l (92 mg/dl)
	M:3% E:3%	Urine:	blood+, pus cells 8-10/ hpf, RBCs 4-6/hpf
Platelets:	257 × 10 ⁹ /l	ECG:	sinus rhythm, mild lateral ischaemia
ESR:	89 mm in 1st hour		
Sodium:	142 mmol/l		
Potassium:	4.2 mmol/l		

QUESTIONS

- Q.1.** What is the most likely diagnosis?
- Q.2.** What further investigations are required?
- Q.3.** Why did the patient complain of pain in the right lumbar region?
- Q.4.** What treatment can be offered?

ANSWERS

- A.1.** In an old male patient, with a history of weight loss, malaise, bone pains, symptoms of prostatism and clinically enlarged prostate with obliteration of median sulcus and adherent rectal mucosa goes in favour of carcinoma of prostate, probably, with bony metastases.
- A.2.**
- i. X-ray of thoracic cage and lumbo sacral spine to show evidence of metastasis which are sclerotic in nature.
 - ii. Serum acid phosphatase (acid labile) which is high.
 - iii. Radio-isotope bone scan to show hotspots of osteosclerotic metastases.
 - iv. Prostatic specific antigen (PSA) is usually raised.
 - v. Prostatic biopsy.
 - vi. Serum calcium and alkaline phosphatase.
- A.3.** This may be due to hydronephrosis on the right side. If the tumor is quite enlarged, it produces obstruction to the uretero vesical orifice resulting in back pressure.
- A.4.**
- i. Oestrogen preparations are given, but these cause gynaecomastia.
 - ii. Sub-capsular bilateral orchidectomy is also beneficial.
 - iii. Cytotoxic therapy including 5-fluorouracil and cyclophosphamide may induce remissions in some patient with endocrine resistant prostatic cancer.
 - iv. Antiandrogens, e.g., cyproterone or flutamide seem to increase median survival.
 - v. Luteinising hormone-releasing hormone (LH-RH). Analogues, such as buserelin or goserilin, are equally effective.
 - vi. Radical prostatectomy which is a major procedure.
 - vii. Brachytherapy: Insertion of radium needles in the prostatic tissue which is managed by computerized three-dimensional localization.
- NB:** The outcome of the tumour depends upon Gleason's scoring which is 1 to 10. Score 1 to 4 (well differentiated), Score 5 to 7 (intermediately differentiated) and score 8 to 10 (poorly differentiated). The lesser the score, the better is the prognosis.

Acute Pyelonephritis

BRIEF HISTORY

A 45-year-old woman presented to the accident and emergency department with a one-day history of severe pain in the left side of her loin which radiated to the left inguinal region. The pain was accompanied by high-grade fever and rigours. She also noticed decreased amount of urine and burning sensation after passing urine. She had lost her appetite and felt nauseated most of the time but also vomitted twice some bilious fluid. She was diabetic and was on oral hypoglycaemic agents. She admitted that she was not punctual to take her medicines regularly.

IMPORTANT CLUES ON CLINICAL EXAMINATION

On examination, she was in obvious discomfort and had a temperature of 104°F. She looked pale and sweaty. There was no cyanosis, jaundice clubbing, lymphadenopathy or oedema. Her pulse was 120 per minute and regular. BP was 140/85 mmHg. Chest and cardiovascular examinations normal. She was tender in the left lumbar region but there was no visceromegaly. Neurological examination did not reveal any abnormality except mild background retinopathy on fundoscopic examination.

INVESTIGATIONS

Following investigations were performed:

Hb :	12.5 g/dl	Chloride:	99 mmol/l
	(normocytic	Blood urea:	6.5 mmol/l (39 mg/dl)
	normochromic)	Creatinine:	84 umol/l (0.9 mg/dl)

Contd...

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WCC:	18.5 × 10 ⁹ /l	Blood sugar:	16 mmol/l (288 mg/dl)
	P:82% L:14%	Urine:	sugar++, albumin+,
	M:2% E:2%		few white cell casts,
Platelets:	340 × 10 ⁹ /l		bacteria++
ESR:	40 mm in 1st hour	ECG:	normal
Sodium:	140 mmol/l	Chest X-ray:	normal
Potassium:	3.8 mmol/l		
Bicarbonate:	25 mmol/l		

QUESTIONS

- Q.1.** What is the most likely diagnosis?
- Q.2.** What is the differential diagnosis?
- Q.3.** What are the commonest organisms involved?
- Q.4.** Discuss predisposing factors causing this disease.

ANSWERS

- A.1.** In a diabetic patient who develops severe lumbar pain, fever and rigours with tenderness in flanks and evidence of leukocytosis on blood examination with pus cells and white cell casts in the urine strongly suggest a diagnosis of acute pyelonephritis which is quite common in females, especially if they are poorly-controlled diabetics as well.
- A.2.** It should be differential from:
- Renal colic due to stones.
 - Papillary necrosis.
 - Renal infarction.
- A.3.**
- Escherichia coli* Ninety percent
 - Proteus*
 - Klebsiella*
 - Pseudomonas*
 - Candida*
 - Streptococcus faecalis*
- A.4.**
- Sex:** Females are commonly affected than males due to different anatomical reasons.
 - Pregnancy:** About 2.8 percent of pregnant women are affected with urinary tract infections.
 - Obstructive uropathy:** Tumour, stricture, stone, posterior ureteral valve or prostatic hypertrophy predispose to more frequent urinary tract infection due to stasis.
 - Neurogenic bladder dysfunction:** Spinal cord injury, tabes dorsalis, multiple sclerosis, diabetes and other diseases may be associated with urinary tract infection.
 - Vesicoureteric reflux:** It is a common cause of recurrent UTIs in children.
 - Renal diseases:** Diabetic nephropathy, gout, nephrocalcinosis, sickle cell disease, hypercalcaemia and hypokalaemia predispose to UTI.
- Urinary tract instrumentation in the form of catheterization, cytосcopy, etc.

Polycystic Kidneys

BRIEF HISTORY

A 43-year-old male presented to the accident and emergency department with a two-day history of pain in his right flank. Thereafter, he passed dark-coloured urine. Two months ago, he had pain in his left flank which was relieved by analgesics. He had been quite well in the past and on two occasions was told that he had high blood pressure. There was no history of diabetes mellitus. He smoked ten cigarettes a day.

IMPORTANT CLUES ON CLINICAL EXAMINATION

On examination, he was in distress. Temperature was 102°F. Pulse was 110 per minute and regular and blood pressure was 150/90 mmHg. General physical examination was normal. Abdominal examination revealed tenderness in the right lumbar region with a mass palpable which had an irregular surface. In the left loin, a similar mass was also palpable but with smooth surface. Systemic examination including cardiovascular, respiratory and central nervous system were all normal.

INVESTIGATIONS

Investigations included:

Hb :	15.4 g/dl (normocytic normochromic)	Potassium:	3.9 mmol/l
		Bicarbonate:	25 mmol/l
		Chloride:	101 mmol/l
WBC	$18.5 \times 10^9/l$ P:88% L:19% M:2% E:1%	Blood urea:	19.2 mmol/l (115 mg/l)
		Creatinine:	146 μ mol/l (1.6 mg/l)
		Urine:	10-15 pus cells/hpf protein ++, blood++
Platelets:	$300 \times 10^9/l$		
ESR:	10 mm in 1st hour		
Sodium:	136 mmol/l		

QUESTIONS

- Q.1. What is the probable diagnosis?
- Q.2. What further investigations are required?
- Q.3. What other associations are known with this disease?
- Q.4. What is the mode of inheritance?
- Q.5. What treatment can be offered?

ANSWERS

- A.1.** In this patient who presented with loin pain, haematuria and fever with palpable masses in both lumbar regions, the most probable diagnosis is polycystic disease of the kidney with acute pyelonephritis.
- A.2.**
- i. An ultrasound of abdomen will show polycystic kidneys.
 - ii. Intravenous urography will also demonstrate the same condition in the form of spider-like calyceal system.
 - iii. Radioisotope scanning may also demonstrate the cysts.
 - iv. CT scan of abdomen.
- A.3.**
- i. Hepatic cysts are present in about 32 percent of the patients. Cysts may also occur in spleen, pancreas, lungs, ovaries, testes, epididymis thyroid, uterus, broad ligament and bladder.
 - ii. Intracranial aneurysms may be associated and can cause fatal haemorrhage.
 - iii. Hepatic fibrosis.
 - iv. Mitral valve prolapse.
 - v. Diverticulosis.
- A.4.** The adult form of the disease is inherited as autosomal dominant. The infantile and childhood form is inherited as autosomal recessive.
- A.5.** Basically, it is the treatment of complications like infection, obstruction and hypertension and management of chronic renal failure.
- The cysts are laid open in some cases (Rovsing's operation) but recurrent episodes of pyelonephritis warrant nephrectomy.

Rheumatoid Arthritis

BRIEF HISTORY

A 59-year-old lady was admitted to the hospital with a twelve-week history of morning stiffness, pain and swelling of both hands and knees. She also complained of malaise, tiredness and difficulty in walking, cooking, dressing and making her own bed. There was no history of fever or cough, but she did complain of dyspnoea on exertion, dryness of mouth and irritation in her eyes.

IMPORTANT CLUES ON CLINICAL EXAMINATION

On examination, she looked unwell and anaemic; her pulse was 78 per minute and regular, and blood pressure 170/100 mmHg. There was no clubbing; no subcutaneous nodules; JVP was not raised; thyroid and lymph nodes were not palpable. She had bilateral symmetrical swelling of metacarpophalangeal and proximal interphalangeal joints. Both knee joints were also swollen with painful limitation of the movements. She could walk only a few steps with the help of two attendants because of pain in her knees. Other joints including shoulder, elbow, hip and ankle were normal. Cardiovascular, respiratory, and abdominal examinations were normal, and there were no neurological abnormalities.

INVESTIGATIONS

The results of initial investigations were:

Hb :	9.5 g/dl	Chloride:	101 mmol/l
	(normocytic	Blood sugar:	6.3 mmol/l (113 mg/dl)
	normochromic)	Blood urea:	12 mmol/l (72 mg/dl)

Contd...

Contd...

WCC:	8.3 × 10 ⁹ /l	Creatinine:	116 umol/l (1.3 mg/dl)
	P:68% L:28%	Urine:	proteins+, 8-10 pus cells/hpf
	M:2% E:2%	ECG:	left axis deviation with strain pattern in lateral chest leads
Platelets:	270 × 10 ⁹ /l	Chest X-ray:	left costo-phrenic angle obliterated
ESR:	53 mm in 1st hour		
Sodium:	143 mmol/l		
Potassium:	4.4 mmol/l		
Bicarbonate:	24 mmol/l		

QUESTIONS

- Q.1. What is the most likely diagnosis?
- Q.2. What three further investigations will you ask for?
- Q.3. What are the ocular complications of this disease?
- Q.4. Give five factors contributing to anaemia in this disease.
- Q.5. What is palindromic rheumatism?
- Q.6. What is Felty's syndrome?
- Q.7. Name four pulmonary complications of diagnosed condition.

ANSWERS

- A.1.** The most likely diagnosis is rheumatoid arthritis. Rheumatoid arthritis can commence at a late age in some patients, and is about three times more common in females. Subcutaneous nodules and vasculitic skin lesions are less commonly seen in South Asian patients with rheumatoid arthritis than in Western countries.
- A.2.**
- i. X-rays of both hands and knees.
 - ii. Rheumatoid factor
 - iii. Aspiration of synovial fluid from the swollen knee joint and analysis of the obtained fluid.
- A.3.**
- i. Episcleritis.
 - ii. Scleritis.
 - iii. Sclero malacia perforans.
 - iv. Kerato conjunctivitis sicca (Sjögren's syndrome).
 - v. Uveitis.
 - vi. Cataracts due to prolonged oral corticosteroid therapy in rheumatoid arthritis.
- A.4.**
- i. Bone marrow depression due to the inflammatory disease.
 - ii. Gastrointestinal blood loss due to drugs, especially nonsteroidal anti-inflammatory drugs and steroids.
 - iii. Poor appetite and general nutrition.
 - iv. Decreased ability to utilise bone marrow iron.
 - v. Some patients may develop secondary amyloidosis affecting the kidneys, and this can result in decreased erythropoietin levels.
- A.5.** Palindromic rheumatism is characterised by recurrent attacks of arthritis of abrupt onset, lasting a few days with periarticular inflammation but no residual joint deformity. The condition is distinctly different from rheumatoid arthritis, but some of these patients may eventually develop rheumatoid arthritis.
- A.6.** This syndrome is described in rheumatoid arthritis when there is splenomegaly and secondary hypersplenism. Some patients may also show lymphadenopathy, pigmentation and leg ulcers.

- A.7.**
- i. Pleural effusion.
 - ii. Pulmonary fibrosis.
 - iii. Pulmonary nodules (if they occur in a person who also has pneumoconiosis the name given is Caplan's syndrome).
 - iv. Bronchiolitis obliterans.

The last complication can present as an obstructive airway disease, while fibrosis presents as restrictive pattern.

NB: Methotrexate and cyclosporin are treatments of choice as disease modifying agents.

Temporal Arteritis

BRIEF HISTORY

A 68-year-old lady was referred to the outpatient clinic with two month history of aches and pains in the shoulders and hip girdles bilaterally, and occasional headaches since the death of her husband. Her symptoms were not relieved by paracetamol and later nonsteroidal anti-inflammatory drugs. There was no history of cough, expectoration, chest pains or palpitation. She had lost about 4 kg weight in the last two months, and complained of left temporal headache for the last three days and occasional blurring of vision in her left eye.

IMPORTANT CLUES ON CLINICAL EXAMINATION

On examination, she looked tired and pale; pulse was 78 per minute and regular, blood pressure was 160/90 mmHg, jugular venous pressure was normal and there was no clubbing, lymphadenopathy, or thyroid enlargement. She was noted to have bruising over her left temporal region with localised hair loss and tenderness and diminished pulsation of her left temporal artery. Ophthalmoscopic eye examination was normal. Cardiopulmonary, abdominal, and neurological examinations were also normal.

INVESTIGATIONS

Laboratory investigations including Hb, ESR, chest X-ray, liver function tests and urea and electrolytes were requested and she was asked to attend again after a week for review with the results of all the investigations.

Her Hb was reported as 10.6 g/dl and the ESR was found to be 52 mm in first hour. Two days before her next appointment, she

woke up with moderately severe left temporal headache and impairment of vision in her left eye.

Results of the other investigations were as below:

WBC:	$8 \times 10^9/l$	Chloride:	99 mmol/l
	P:70% L:25%	Blood urea:	8.9 mmol/l (53.4 mg/dl)
	M:3% E:2%	Creatinine:	140 μ mol/l (1.5 mg/dl)
Platelets:	$370 \times 10^9/l$	Blood sugar:	6.1 mmol/l (110 mg/dl)
Sodium:	139 mmol/l	Urine:	normal
Potassium:	4.1 mmol/l	Chest X-ray:	heart size normal, lungs
Bicarbonate:	25 mmol/l		fields were clear.

QUESTIONS

- Q.1. What is the most likely diagnosis?
- Q.2. What course of action would have you taken if you had seen her on her first visit?
- Q.3. Is the finding of an ESR of 52 mm in first hour not consistent with the diagnosis?
- Q.4. How do you treat such a patient?
- Q.5. Name a few associated clinical manifestations of your most likely diagnosis.

ANSWERS

- A.1.** The most likely diagnosis in this lady presenting with headaches and painful shoulder and hip girdles and tenderness over her left temporal region is temporal arteritis.
- A.2.** Instead of waiting to see her again after a week, she should have been immediately treated, because of a strong clinical suspicion of temporal arteritis, with a moderately high starting dose of oral corticosteroids, and if possible an urgent temporal artery biopsy would be advisable. This condition is one of the medical emergencies and delay in diagnosis and treatment can result in permanent loss of vision. This patient is so classical that treatment should have been started while waiting for the temporal artery biopsy. It is best to have a pathological diagnosis, but some physicians may not require a temporal artery biopsy in this patient if it is not easy to find a competent person to do the biopsy and/or the pathology department is not staffed by competent and conscientious pathologists, because the biopsy needs to be examined thoroughly with “cuts” throughout the full segment of the biopsy because of “skip lesions”. A “negative” biopsy would not exclude the diagnosis of temporal arteritis in this patient.
- A.3.** No, Although in most cases the ESR is above 80 mm, this is not invariably the case. An ESR of 52 mm does not rule out the diagnosis. At the same time, it is important to remember that in many elderly an ESR of 40 to 50 mm may not be associated with any significant disease process. A few patients with biopsy proven temporal arteritis and normal ESR have been reported, but this is a very rare occurrence.
- A.4.** Patients with temporal arteritis should be treated with high-dose steroids, about 60 mg prednisone per day; the dose is later adjusted according to the falling ESR and symptomatic relief. The fall in ESR is usually very dramatic, noticeably within three to six days and it further strengthens the clinical impression of temporal arteritis. The total time required for this therapy is variable, usually for a year, although some patients may need to be treated for a longer period that may extend from two to three years.

- A.5.** The arteritic process may not be localised only to the temporal arteritis. Therefore, it is better to call it giant cell arteritis, based on the histological findings, rather than temporal arteritis. Recent studies suggest evidence of inflammation of the aorta in one-third of patients; and aortic aneurysm and dissection of the aorta have been reported. Mesenteric arteritis, myocardial infarction and claudication of the jaw and lower extremities are attributed to temporal arteritis in some patients. Mononeuritis multiplex and pyrexia of unknown origin are also among other associations.

Polyarteritis Nodosa

BRIEF HISTORY

A 48-year-old man presented to the outpatient clinic with undue fatigue, malaise and general aches and pains. There was history of coughing up small quantities of blood for the last eight weeks. In between the attacks of haemoptysis, he had been coughing up yellowish sputum. On further questioning, he admitted that he was becoming increasingly short of breath and had occasional wheeze. He had lost about 5 kg of weight in the last two months and noticed a poor appetite. There was no history of diabetes or hypertension or any other serious illness in the past. He smoked 15 to 20 cigarettes per day and was on no medications. There was no family history of such illness either. His last physical examination eight months ago, was completely normal. Three years ago he had blood transfusions followed by an episode of jaundice.

IMPORTANT CLUE ON CLINICAL EXAMINATION

On examination, he looked ill, but there was no pallor, cyanosis, jaundice or peripheral oedema. He had a temperature of 102.4°F. His pulse was 98 per minute and regular and BP was 145/90 mmHg. Heart sounds were normal. Chest examination revealed a few scattered crackles with occasional rhonchi. Abdominal and neurological examinations were normal.

He had been given antibiotics, bronchodilators and steam inhalation but did not show much improvement after a week, he continued to have low-grade fever and was spitting little amount of fresh blood. On this basis, he was hospitalized and on the second day of admission he started having retrosternal chest pain more marked while lying down. This time he also complained of aches and pains all over his body, more so in the joints. Repeat examination

revealed a temperature of 99.8°F, pulse was 100 per minute and BP was 170/105 mmHg. On auscultation, there was a scratchy noise in the precordium besides crackles and rhonchi in the chest. There was no clinical evidence of arthritis.

INVESTIGATIONS

Following investigations were ordered.

Hb :	12.8 g/dl (normocytic normochromic)	Potassium:	4.2 mmol/l
		Bicarbonate:	26 mmol/l
		Chloride:	102 mmol/l
WBC:	$11 \times 10^9/l$ P:74% L:17% M:3% E:6%	Blood urea:	12 mmol/l (72 mg/dl)
		Creatinine:	140 μ mol/l (1.5 mg/dl)
		Blood sugar:	8 mmol/l (144 mg/dl)
ESR:	58 mm in 1st hour	LFT's:	normal
Sodium:	140 mmol/l		

QUESTIONS

- Q.1. What is the most likely diagnosis?
- Q.2. What is the differential diagnosis?
- Q.3. What further investigations are necessary?
- Q.4. How would you confirm the diagnosis?
- Q.5. Is cutaneous involvement observed in most patients?
- Q.6. What treatment is recommended?

ANSWERS

- A.1.** In a male with a history of haemoptysis, fever, raised blood pressure, raised ESR and elevated urea, arthralgia and myalgia and a past history of jaundice raise the possibility of polyarteritis nodosa (PAN) probably associated with hepatitis B infection.
- A.2.** This should be differentiated from:
- i. Hypertension.
 - ii. Wegener's granulomatosis (C-ANCA).
 - iii. Goodpasture's syndrome.
 - iv. Pulmonary tuberculosis with renal involvement.
 - v. Carcinoma of bronchus.
 - vi. Sarcoidosis.
- A.3.**
- i. Full urine examination including sediments and microscopic haematuria.
 - ii. ECG.
 - iii. Chest X-ray.
 - iv. Sputum for AAFB and malignant cells.
 - v. Creatinine clearance.
 - vi. Hepatitis B and C serology.
 - vii. P-ANCA.
- A.4.** It is done by more invasive investigations like:
- i. Coeliac and renal artery angiogram to look for micro-aneurysms.
 - ii. Renal biopsy for evidence of arteritis and glomerulonephritis if evidence of glomerular involvement, but it is quite risky in these patients.
- A.5.** Most patients with classical PAN do not have skin involvement, however, these include:
- i. Nodules.
 - ii. Rashes (non-specific).
 - iii. Urticaria.
 - iv. Erythema multiforme.
 - v. Purpura.
 - vi. Infarcts.
 - vii. Livedo reticularis.
 - viii. Raynaud's phenomenon.

- A.6.** Corticosteroids may be helpful in some cases. Initially, high doses are given, then it is tapered off very gradually. The first three months appear to be the most crucial. Those patients who get a remission on therapy rarely suffer from recurrent vasculitis.

BRIEF HISTORY

A 58-year-old gentleman was referred to the outpatient clinic with a history of painless swelling over his right elbow which he had noticed four weeks prior to his visit. He denied any history of trauma. In the past, he had always had good health. He smoked ten cigarettes a day. He also had one to two units of whisky on most evenings for the last few years. He was fond of eating meat, chicken etc.

IMPORTANT CLUES ON CLINICAL EXAMINATION

On examination, he was obese, his blood pressure was 180/100 mmHg, pulse was 78 per minute and regular. JVP was normal. There was no clubbing, lymphadenopathy or thyroid enlargement. The swelling overlying his olecranon was about two centimetres in diameter, soft, non-tender and fluctuant. The temperature and the colour of the overlying skin was normal. Movements of the elbow joints and examination of the other joint were normal. Over his left ear, he was noted to have two small nodules which were whitish pale in colour, firm and non-tender. Apex beat localized in the left fifth intercostal space inside mid-clavicular line. His heart sounds were normal. Trachea was central, there was normal chest expansion and air entry was equal on both sides. Liver edge was just palpable. Examination of central nervous system was unremarkable.

INVESTIGATIONS

Following investigations were performed:

Hb :	12.8 g/dl	Blood glucose: 7.8 mmol/l (140 mg/dl)
	(normocytic	Blood urea: 11.4 mmol/l (68 mg/l)
	normochromic)	Creatinine: 130 umol/l (1.4 mg/dl)

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WCC:	9.8 × 10 ⁹ /l	Protein:	6.8 g/dl
	P 74% L 20%	Albumin:	3.8 g/dl
	M 4% E 2%	Bilirubin:	17 umol (1 mg/dl)
Platelets:	290 × 10 ⁹ /l	Urine:	normal
ESR:	26 mm in 1st hour	ECG:	normal
Sodium:	139 mmol/l	Chest X-ray:	with in normal limits
Potassium:	4.1 mmol/l		
Bicarbonate:	24 mmol/l		
Chloride:	99 mmol/l		

QUESTIONS

- Q.1. What is the most likely diagnosis, and why?
- Q.2. What are the other common causes of bursitis?
- Q.3. What two investigations would you ask for?
- Q.4. Name four commonly associated conditions with your diagnosis.
- Q.5. Name three drugs which are commonly used for the treatment.
- Q.6. What is podagra?
- Q.7. What is pseudogout and how does it differ from gout?
- Q.8. Is test of uric acid necessary?

ANSWERS

- A.1.** The most likely diagnosis is gouty olecranon bursitis. The presence of nodular gouty tophi over his left ear is highly suggestive of tophaceous gout.
- A.2.**
- Traumatic.
 - Sepsis.
 - Rheumatoid arthritis.
- A.3.**
- Aspiration of the swelling and examination of the fluid for microscopy for urate crystals.
 - Aspiration of nodules over the ear to look for urate crystals.
- A.4.**
- Obesity.
 - Diabetes mellitus.
 - Hypertension.
 - Ischaemic heart disease.
- A.5.**
- Allopurinol (not to be used in acute attacks).
 - Probenecid (not to be used in acute attacks).
 - Sulphinpyrazone and other non-steroidal anti-inflammatory agents, e.g., colchicine.
- A.6.** It is the name given to painful, swollen, erythematous, extremely tender and hot metatarso-phalangeal joint of the great toe.
- A.7.** Pseudogout is the name given to acute episode of arthritis triggered by calcium pyrophosphate. The deposition of these crystals in the articular cartilage is recognised as chondrocalcinosis on X-ray and is due to calcium pyrophosphate crystals, which are weakly positive birefringent plump crystals while gout is caused by strongly negatively birefringent crystals which are needle like and are composed of sodium urate.
- A.8.** Uric acid is not of significant consideration. Serum uric acid level does not indicate presence or absence of gout, therefore high levels of uric acid does not mean acute gout. One can have normal uric acid level in 25 percent of patients with acute gout. The serum uric acid level, however, helps determine whether drug therapy is needed for lowering elevated uric acid level, and its dose and duration.

Ankylosing Spondylitis

BRIEF HISTORY

A young man of 28 presented to the outpatient department with a one-year history of gradually increasing low back pain and stiffness. The back stiffness was worse in the morning or after prolonged sitting. For the last three months, he had been experiencing anterior chest pain and tenderness. He also had noticed that it was difficult for him to bend forward and pick up things from the floor. He had not suffered from any serious illness in the past. There was no history of hypertension or diabetes either.

IMPORTANT CLUES ON CLINICAL EXAMINATION

On examination, he was of medium built, pulse 78 per minute, BP 125/85 mmHg, with a normal general physical examination, but his chest expansion was diminished and he had pain on full inspiration. His manubriosternal area and some of the costochondral junctions were somewhat tender on firm pressure. He had limited movements of the lumbar spine and tenderness on both sacroiliac joints. Central nervous system examination did not reveal any abnormality.

INVESTIGATIONS

Following investigations were performed:

Hb :	13.4 g/dl (normocytic normochromic)	Potassium:	4.6 mmol/l
		Bicarbonate:	25 mmol/l
		Chloride:	99 mmol/l
WBC:	$7.8 \times 10^9/l$	Blood urea	5.6 mmol/l (34 mg/l)
	P: 74% L: 22%,	Creatinine:	110 μ mol/l(1.2 mg/dl)
	M: 2% E: 2%	Urine:	normal

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Platelets:	$320 \times 10^9/l$	Chest X-ray:	normal
ESR:	54 mm in 1st hour		
Sodium:	136 mmol/l		

QUESTIONS

- Q.1. What is the most likely diagnosis?
- Q.2. What further investigations are indicated?
- Q.3. What are enthesitis and syndesmophytes?
- Q.4. Discuss the differential diagnosis.
- Q.5. What treatment can be offered?
- Q.6. Is this disease associated with any HLA allele?

ANSWERS

A.1. In a young individual, male or female, with a history of chronic backache and difficulty in bending, along with restricted movements of spine and tender sacroiliac joints indicates ankylosing spondylitis.

A.2. These include:

- i. Radiograph of the pelvis to look for sacroiliitis.
- ii. Radiographs of thoraco-lumbar spine to find the extent of radiographic abnormalities in the spine.

N.B: HLA-B27 is not needed in such a patient when there is radiographic evidence of sacroiliitis that confirms the diagnosis of ankylosing spondylitis. This test can sometimes be helpful when radiographic findings are equivocal (not clear-cut), as it is present in more than 85 percent of patients with ankylosing spondylitis and 4 to 8 percent of the general population in Pakistan.

A.3. *Enthesitis*: Inflammation occurring at the point of bony attachment of tendons, ligaments, and joint capsule.

Syndesmophytes: Ossification of superficial layers of annulus fibrosis that leads to bony bridging between vertebral bodies.

A.4. It should be differentiated from:

- i. Enteropathic arthritis—Associated with ulcerative colitis and regional enteritis.
- ii. Reiter's syndrome and psoriatic arthritis—Distribution of syndesmophytes is more random and extends beyond the vertebral margin.
- iii. Diffuse idiopathic skeletal hyperostosis (DISH) or Forestier disease—no involvement of appophyseal and sacroiliac joints, although the capsules of these joints may show ossification.

A.5. The main aim is to prevent deformities by regular exercises and, therefore, the patient should be properly guided about it.

The patient should keep an erect posture and sleep in prone position or supine position on a hard bed with the thinnest pillow if possible. Spinal range of motion and breathing

exercises should be encouraged, and smoking should be avoided. The patient should also avoid fall or injury because of high risk of spinal fracture.

Non-steroidal anti-inflammatory drugs, e.g., indomethacin, naprosyn, or diclophenac.

Surgical correction of spinal deformities is recommended in rare circumstances. Patients with crippling hip disease may get enormous relief by total hip replacement.

Systemic Lupus Erythematosus

BRIEF HISTORY

A 24-old-female presented with a two week history of painful ulcers in her mouth, fever, weight loss, painful ankles, weakness, undue fatigue and difficulty in keeping with daily routine. She had been married for eight months. She had also complained of loss of appetite and had lost almost 4 kg of weight during the last five weeks. She also noticed that her hair were falling off quite easily. There was no history of chest pain, cough, expectoration or palpitation. She had experienced some stiffness in both hands and excessive redness over her cheeks for the last ten days. She had no previous illnesses apart from occasional migraine type headaches that she had suffered for the last three years. There was no such family history and no allergies were known either.

IMPORTANT CLUES ON CLINICAL EXAMINATION

On examination, she looked unwell and anxious. Temperature was 103.5°F. Her blood pressure was 115/80 mmHg. Pulse was 110 per minute and regular. She looked pale but there was no jaundice, clubbing or cyanosis. A few lymph nodes were palpable in the right and left supra-clavicular region. She had an erythematous rash over her face covering both cheeks and the centre of her nose. Her mouth examination revealed superficial non-apthous ulcers on the lips, tongue, hard palate and nasal mucosa. Joints of both hands and ankles were warm to touch and slightly tender. She also had reddish lesions over her both shin. Her chest was clear. Heart sounds were normal with no murmur. Spleen was just palpable on deep inspiration and was non-tender. Liver was not palpable and there was no ascites. Neurological examination was completely normal.

INVESTIGATIONS

Following were the results of various investigations:

Hb:	11.9 g/dl (normocytic normochromic)	Blood sugar:	5.5 mmol/l (100 mg/dl)
		Blood urea:	7.7 mmol/l (46 mg/dl)
		Creatinine:	110 μ mol/l (1.2 mg/dl)
WCC:	8.8×10^9 /l P: 69% L: 27% M: 1% E: 3%	Serum bilirubin	18 μ mol/l (1.1 mg/dl)
		Total Oproteins:	5.0 g/dl
		Albumin:	3.0 g/dl
Platelets:	200×10^9 /l	Urine analysis:	protein ++, pus cells 2-4/ hpf, hyaline and granu- lar casts+
ESR:	20 mm in 1st hour		
Sodium:	136 mmol/l	ECG:	normal
Potassium:	3.9 mmol/l		
Bicarbonate:	25 mmol/l		
Chloride:	101 mmol/l		

QUESTIONS

- Q.1.** What is the most likely diagnosis and why?
- Q.2.** What is the criteria for diagnosing this disease?
- Q.3.** What further four investigations will help your diagnosis?
- Q.4.** Name three drugs which may be used to treat this condition.
- Q.5.** Name a few drugs which can cause similar symptoms and signs.
- Q.6.** What is the role of plasmapheresis in the treatment of this disease?
- Q.7.** What are the skin manifestations of this disease?

ANSWERS

- A.1.** The most likely diagnosis in this young woman with a history of weight loss, arthralgia, fatigue, weakness, mouth ulcers, skin lesion over her face (Butterfly rash), renal involvement, lymphadenopathy and splenomegaly is systemic lupus erythematosus (SLE).
- A.2.** The local clinical features of SLE have a wide variability in different patients. The American Rheumatism Association (ARA) recommendations suggest a minimum of four of the following features:
- i. Malar rash
 - ii. Discoid lupus
 - iii. Photosensitivity
 - iv. Oral ulceration
 - v. Arthritis
 - vi. Serositis
 - vii. Renal disorders:
 - a. Proteinuria > 0.5 G/day
 - b. > 3+ dipstick proteinuria
 - c. Cellular casts.
 - viii. Neurological diseases
 - a. Seizures
 - b. Psychosis.
 - ix. Haematological disorders:
 - a. Haemolytic anaemia
 - b. Leucopenia < 4000/ul
 - c. Lymphopenia < 1500/ul
 - d. Thrombocytopaenia < 100,000/ul:
 - i. Positive ANA
 - ii. Immunological abnormalities.
 - e. LE cells
 - f. Antibodies to native DNA or
 - g. Antibody to Sm or
 - h. False positive serological tests for syphilis.

If four of these nine criteria are present at any time during the disease, the diagnosis of SLE is confirmed.

- A.3.**
- i. ANA.
 - ii. Anti-double stranded DNA antibody.

- iii. Serum complement estimation.
 - iv. Chest X-ray.
- A.4.
 - i. Corticosteroids
 - ii. Chloroquine or hydroxychloroquine
 - iii. Azathioprine or other immunosuppressant drugs.
Experimental treatments include intravenous gamma globulins, cyclosporin, immunoadsorption, photo-chemotherapy, nodal irradiation and various monoclonal antibodies.
- A.5. These include:
 - i. Hydralazine
 - ii. Procainamide
 - iii. Isoniazid
 - iv. Quinidine
 - v. Chlorpromazine
 - vi. Methyl dopa.
- A.6. Plasmapheresis has been tried as an adjunct to treatment with corticosteroids with SLE patients with vital organ involvement that is resistant to conventional therapy. This procedure is quite expensive and involves removal of immune complexes from the blood and allows immunologic clearance mechanisms to act appropriately.
- A.7. Apart from butterfly rash, the skin can be involved in the form of discoid lupus, sub-acute cutaneous lupus erythematosus, urticaria, bullae, erythema multiforme, lichen planus like lesions and vasculitic skin lesions which include purpura, subcutaneous nodules, nail fold infarcts, ulcers, panniculitis and gangrene of digits and full blown Stevens-Johnson syndrome.

*Scabies***BRIEF HISTORY**

A 25-year-old bus driver presented to the outpatient department with a two week history of itchy rashes around his hands, fingers and inguinal region. His itching was worse at night and he had difficulty in sleeping at times. He had enjoyed good health and had not been ill since he remembered. He smoked 20 cigarettes a day. He was taking no drugs. His wife and one son had also been complaining of itching all over for the last five days.

IMPORTANT CLUES ON CLINICAL EXAMINATION

On examination, he appeared fit and healthy. JVP was normal. Blood pressure was 140/90 mmHg. Pulse was 80 per minute and regular. There was no anaemia, cyanosis, jaundice, clubbing or oedema. Lymph nodes were not enlarged. On his hands, he had fine, dark lines of scratching and eczematoid papular rashes in the finger webs. There were similar rashes over his inguinal area and scrotum. A few crusty lesions were also present on glans penis.

INVESTIGATIONS

Results of the following investigations were available:

Hb :	14.2 g/dl	Blood sugar:	7.2 mmol/l (130 mg/dl)
	(normocytic	Blood urea:	6 mmol/l (36 mg/dl)
	normochromic)	Creatinine:	86 umol/l (1.1 mg/dl)
WCC:	$9.4 \times 10^9/l$	Urine analysis:	normal
	P:66% L:26%	ECG:	normal
	M:2% E:6%	Chest X-ray:	normal
Platelets:	$240 \times 10^9/l$		

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ESR:	12 mm in 1st hour
Sodium:	139 mmol/l
Potassium:	3.8 mmol/l
Bicarbonate:	25 mmol/l
Chloride:	101 mmol/l

QUESTIONS

- Q.1.** What is the most likely diagnosis?
- Q.2.** How would you confirm the diagnosis?
- Q.3.** Name three drugs which may be used to treat this condition.
- Q.4.** What is the relationship of this condition to Norway?

ANSWERS

- A.1.** The most likely diagnosis in this young patient with pruritic lesions on his hands and fingers spreading to his family members is scabies. Scabies is probably the most common skin condition associated with poor living standards. It may sometimes be difficult to diagnose because scratching and secondary infection make the characteristic burrows in the finger webs difficult to recognize. The parasite causing scabies is the mite *sarcoptes scabiei*.
- A.2.** Examination of the skin scrapings, using 10 percent potassium hydroxide to demonstrate the parasite is a reliable method of establishing the diagnosis. The mite itself or the eggs may be seen in the film. Although the involved person may harbour millions of mites, but average number of female mites per infection is eleven.
- A.3.** i. Gamma Benzene Hexachloride (1% cream).
ii. Benzyl Benzoate (25% emulsion).
iii. Eurax (Crotamiton) cream.
It is important to remember that all the members of the family should be treated simultaneously. Improvement in general living conditions and personal hygiene are also important in the prevention of re-infection.
- A.4.** This is particularly a virulent infestation. Millions of mites may be present producing a highly infectious exfoliative dermatitis. There was an epidemic of such infestation in the prisoners who were kept in jails in Norway due to very poor hygienic conditions. It is also called Norwegian scabies.

Infectious Mononucleosis

BRIEF HISTORY

A man of 24 was admitted with five-day history of malaise, generalised pains and bodyaches, headaches and sore throat. For the last two days he had stopped eating, drinking and complained of difficulty in swallowing. He had no chest pain or palpitations. There were no urinary or bowel symptoms. He was single and was a student of engineering, living in the hostel.

IMPORTANT CLUES ON CLINICAL EXAMINATION

On examination, his temperature was 103°F. His throat was congested and he was dehydrated. Cervical and axillary lymph nodes were palpable which were discrete and moderately tender. There was no clubbing, anaemia, jaundice or oedema. He was a bit confused and disorientated. Blood pressure was 140/95 mmHg and pulse was 92 per minute and regular. Spleen was 2 cm enlarged. Liver was not palpable and there was no ascites. Apart from confusion, his neurological examination was normal.

INVESTIGATIONS

Following results were available:

Hb :	14.2 g/dl (normocytic normochromic)	Sodium:	144 mmol/l
		Potassium:	3.8 mmol/l
		Bicarbonate:	23 mmol/l
WCC:	$14 \times 10^9/l$ P: 40% L: 58% M: 1% E: 1% (Few atypical lymphocytes)	Chloride:	100 mmol/l
		Blood sugar:	6.2 mmol/l (112 mg/dl)
		Blood urea:	8.6 mmol/l (52 mg/dl)
		Creatinine:	98 μ mol/l (1.1 mg/dl)
		Urine:	normal
Platelets:	$320 \times 10^9/l$	ECG:	sinus tachycardia,
ESR:	38 mm in 1st hour	Chest X-ray:	normal

QUESTIONS

- Q.1.** What is the most likely diagnosis?
- Q.2.** What two investigations will confirm the diagnosis?
- Q.3.** Give three serious complications of this condition.
- Q.4.** Can this disease affect the elderly?
- Q.5.** Why ampicillin is not recommended in this disorder?
- Q.6.** List the differential diagnosis.

ANSWERS

- A.1.** The most likely diagnosis in this young man with flu-like illness, throat congestion, pyrexia, lymphadenopathy, splenomegaly and leucocytosis with high lymphocytic count and atypical lymphocytes is infectious mononucleosis.
- A.2.** i. Paul-Bunnell test for heterophil antibodies.
ii. Antibody to Epstein-Barr virus (rising titres).
- A.3.** i. Guillain-Barre' syndrome
ii. Respiratory distress due to pharyngeal oedema.
iii. Autoimmune haemolytic anaemia.
- A.4.** Though infectious mononucleosis characteristically affects the children and young adults, but elderly patients may also be affected as shown by a number of recent reports in which older people were involved.
- A.5.** Macular or maculopapular rash has been noticed with the use of ampicillin.
- A.6.** i. Exudative tonsillitis.
ii. Diphtheria.
iii. Vincent's angina.
iv. Acute leukaemia.
v. Cytomegalovirus (CMV) mononucleosis.
vi. Acute infectious lymphocytosis.
vii. Rubella.
viii. Toxoplasmosis.
ix. Infective hepatitis.

Enteric Fever

BRIEF HISTORY

An 18-year-old girl presented with a ten day history of fever with rigours, headaches and dry cough. The fever started gradually and she felt cold and then developed dry cough. She also felt weaker and had lost appetite. A couple of days prior to her visit to the hospital she developed sudden pain in the left subcostal margin. There was no history of recurrent sore throat or joint pains. She visited quite a few general practitioners, but the fever did not settle.

IMPORTANT CLUES ON CLINICAL EXAMINATION

On examination, she looked tired and anxious. Throat was congested and tongue was coated. Temperature was 102.4°F. Pulse was 84 per minute and regular. BP was 110/70 mmHg. She had no jaundice or lymphadenopathy. Cardiovascular system was normal and so was the chest. Abdominal examination revealed just palpable spleen and tenderness in the left hypochondrium when pressed hard. Neurological examination was normal.

INVESTIGATIONS

Investigations included:

Hb :	11.4 g/dl (normocytic normochromic) no malarial parasites seen	Blood sugar:	5 mmol/l (90 mg/dl)
		Blood urea	4 mmol/l (24 mg/dl)
		Creatinine	88 umol/l (0.9 mg/dl)
		Urine:	normal
		Bilirubin:	24 umol/l (1.2 mg/dl)
WCC:	$5.4 \times 10^9/l$	SGOT:	64 U/l
	P:64% L:32%	SGPT:	80 U/l
	M:2% E:2%	Alk.Phos:	156 U/l

Contd...

Contd...

Platelets:	260 × 10 ⁹ /l	ECG:	sinus rhythm
ESR:	35 mm in 1st hour	Chest X-ray:	normal
Sodium:	138 mmol/l		
Potassium:	4.2 mmol/l		
Bicarbonate:	26 mmol/l		
Chloride:	96 mmol/l		

QUESTIONS

- Q.1. What is probable diagnosis?
- Q.2. What two further investigations are important?
- Q.3. What is the differential diagnosis?
- Q.4. Name a few complications of this disease.
- Q.5. Discuss briefly the therapeutic management of this disease.

ANSWERS

A.1. In a young adult with ten-day history of fever with rigours, severe headache, dry cough, congested throat and coated tongue, possibility of enteric fever is quite high.

A.2. i. Blood cultures At least three sets of blood cultures are required, especially taken at the spike of fever. *Salmonella typhi* may be isolated.

ii. Widal's test The agglutinins begin to appear after about one week and reach a peak titres during third or fourth week, therefore, it signifies the repetition of Widal's test to document rising titres.

Typhidot IgM indicates most recent infection, whereas IgG indicates old infection with *Salmonella typhi*.

A.3. There are many conditions which can resemble typhoid fever, e.g. infective hepatitis, atypical pneumonia, brucellosis, tularemia, psittacosis, infectious mononucleosis, malaria, tuberculosis, lymphoma and rheumatic fever. Typhoid should be considered first on the list.

A.4. Besides weight loss and nutritional deficiencies, the following are the important complications:

i. Intestinal haemorrhage They occur mostly in the second or third week of the disease. A sudden drop in blood pressure and temperature may be the first manifestation of haemorrhage.

ii. Intestinal perforation The incidence is far reduced by the advent of new antimicrobial agents. The commonest site is terminal ileum and is observed during the third week of the disease leading to localised or generalised peritonitis.

iii. Meningitis

iv. Chondritis

v. Periostitis

vi. Osteomyelitis (especially in sicklers)

- vii. Arthritis
- viii. Pyelonephritis
- ix. Pneumonia
- xi. Severe deep thrombophlebitis.

Late complications include:

- i. Peripheral neuritis
- ii. Deafness
- iii. Alopecia
- iv. Haemolytic anaemia especially in glucose-6-phosphate dehydrogenase deficient individual.

A.5. There are many antimicrobial agents which are used for typhoid fever.

- i. Ampicillin and amoxycillin should be used as 1 gram 6 hourly either orally or parenterally for at least three weeks.
- ii. Ofloxacin (Tarivid) and ciprofloxacin (Ciproxin) which are third-generation fluoroquinolone derivatives are quite effective in treating enteric fever. The former is given as 400 mg twice a day for ten days and the latter is given in the dose of 750 mg 12 hourly for ten days.
- iii. Third-generation cephalosporin such as cefotaxim (Claforan), is also used for typhoid fever but at least 6 grams to 8 grams are given daily parenterally and it is very expensive drug to use. Other option is Ceftriaxon (Rocephin) as 2 gm IV bd for five days.
- iv. Chloramphenicol used to be the antibiotic of choice, but nowadays resistant strains have developed. Usual dose is 50 mg/kg per day divided in four doses. When the patient becomes afebrile (usually after 5 to 7 days), then the dose is reduced to 30 mg/kg per day for two weeks. Parenteral therapy can also be given as 1 gram 6 hourly. The side effects of marrow suppression should be kept in mind which can lead to aplastic anaemia. Besides all the above antimicrobial therapy, supportive therapy is also important in the form of nutritional requirements. Role of steroids in moribund patients along with chloramphenicol is mentioned in the literature.

BRIEF HISTORY

A 32-year-old woman attended the outpatient with a two-month history of weight loss, low grade fever, night sweats and anorexia. She also complained of lumps and bumps on both sides of the neck and inguinal region. She was seen by a few doctors and was prescribed medicines but did not respond to this treatment. One month later, in addition to the beginning of the above symptoms she developed cough and whitish lesions on her tongue. She had no illnesses in the past. She was married and had two children by caesarian sections. Her third delivery took place in Saudi Arabia, but she had antepartum haemorrhage and was transfused 4 to 6 units of blood from the local blood bank. There were no allergies noticed.

IMPORTANT CLUES ON CLINICAL EXAMINATION

On examination, she looked toxic, temperature was 99.8°F and blood pressure was 110/70 mmHg. Chest was clear and heart sounds were normal. There was cervical, axillary and inguinal lymphadenopathy and it was painful too. Abdominal and neurological examinations were also normal.

INVESTIGATIONS

She was investigated and following investigations were asked:

Hb :	12.2 g/dl (normocytic normochromic)	Chloride:	96 mmol/l
		Blood urea:	7 mmol/l (42 mg/dl)
		Creatinine:	112 umol/l (1.3 mg/dl)
WCC	$10.2 \times 10^9/l$	Blood sugar:	4 mmol/l (72 mg/dl)
	P:70% L:26%	Urine:	normal
	M:2% E:2%	ECG:	sinus tachyardia

Contd...

Contd...

Platelets:	265 × 10 ⁹ /l	Chest X-ray: normal
ESR:	74 mm in 1st hour	A lymph node FNA was arranged and
Sodium:	140 mmol/l	patient was asked to come in a few days.
Potassium:	3.4 mmol/l	
Bicarbonate:	23 mmol/l	

Five days later she presented to accident and emergency department with high grade fever, extreme weakness, fatigue and further weight loss. She also complained of shortness of breath, cough and chest discomfort. Chest examination revealed a few crackles both lower zones. Chest X-ray requested at that time showed bilateral fine perihilar infiltrates.

QUESTIONS

- Q.1. What is the most likely diagnosis?
- Q.2. What was the likely diagnosis on her second visit?
- Q.3. Discuss the differential diagnosis.
- Q.4. How would you confirm it?
- Q.5. Discuss the management of this disease.
- Q.6. List a few clinical laboratory abnormalities associated with the primary disease.

ANSWERS

- A.1.** In a young female who had a history of low-grade fever, weight loss, cough, anorexia, lymphadenopathy and a history of blood transfusion favours a diagnosis of a chronic infection, but in this case an immunodeficiency syndrome, i.e., AIDS.
- A.2.** This patient was disproportionately out of breath, had fever, chest pain and cough with bilateral perihilar infiltrates, developing pneumonia—probably pneumocystis carinii pneumonia (PCP).
- A.3.** Other causes of pneumonia or coexistent infections, such as tuberculosis, fungal, and cytomegaloviral must be excluded. Bacterial pneumonias can be caused by organisms, e.g., *pneumococci*, *haemophilus*, *Branhamella* and group B *streptococci*. Other possibility is lymphocytic interstitial pneumonitis.
- A.4.** Other investigations include:
- Arterial blood gases (low PO_2).
 - Sputum cytology to see cysts of *P. carinii*.
 - Fibroptic bronchoscopy and bronchial washings/lavage.
 - Monoclonal antibodies to pneumocystis proteins.
 - DNA probing has been developed but not yet in routine use.
- Moreover, enzyme-linked immuno-sorbent assay (ELISA) technique to determine the antibodies against HIV-1 and HIV-2.
- A.5.** The treatment of pneumocystis carinii includes:
- High, dose intravenous co-trimoxazole (Septran) for 2 to 3 weeks.
 - Intravenous pentamidine is the alternative treatment if the patient is intolerant to co-trimoxazole.
 - Atovaquone—a hydroxynaphthoquinone is a more recent addition to the treatment.
 - Adjuvant high-dose corticosteroids (40-60 mg of prednisolone) helps in severe cases of pneumonia.
- Prophylaxis against PCP is recommended, i.e., co-trimoxazole one tablet once a day or DS (double strength) tablet thrice weekly is most effective.

OR dapsons 100 mg orally daily.

OR dapsons 50 mg with pyrimethamine 50 mg weekly is a good alternative.

Nebulized pentamidine is recommended as 300 mg every four weeks.

A.6. The different laboratory abnormalities associated with AIDS are:

- i. Lower CD4-positive lymphocytes (helper)
- ii. Raised CD8-positive lymphocytes (suppressor)
- iii. Anaemia
- iv. Cytopoenias
- v. Raised ESR
- vi. Raised B₂ microglobulins
- vii. Raised IgA
- viii. Lowered cellular immune functions
- ix. Lowered HIV-specific cytotoxicity
- x. Lowered anti p24
- xi. Raised p24
- xii. Raised viral load
- xiii. Raised syncytium—including viral phenotype.

BRIEF HISTORY

A 25-year-old man presented to accident and emergency department with a two-day history of high-grade fever with rigours. The fever started suddenly after he felt extremely cold and followed by profuse sweating. He also noticed that fever was more in the evening and did not get better with antibiotics and paracetamol which was prescribed by a general practitioner. He also noticed passing dark-coloured urine. He never had been ill in the past. He smoked 20 cigarettes per day.

IMPORTANT CLUES ON CLINICAL EXAMINATION

On examination, he looked exhausted. The temperature was 103°F. There was mild tinge of jaundice. There was no pallor, cyanosis, clubbing or lymphadenopathy. Pulse was 104 per minute and regular. BP was 115/75 mmHg. Cardiovascular, respiratory and abdominal examinations were normal. There were no focal signs in the central nervous system.

INVESTIGATIONS

Following investigations were carried out:

Hb :	11.4 g/dl (normocytic normochromic)	Blood urea:	4.5 mmol/l (27 mg/dl)
		Blood sugar:	6.4 mmol/l (116 mg/dl)
		Creatinine:	98 umol/l (1.1 mg/dl)
WCC:	$10 \times 10^9/l$ P:74% L:22% M:2% E:2%	Bilirubin:	27 umol/l (1.6 mg/dl)
		SGOT:	78 U/l
		SGPT:	68 U/l
Platelets:	$290 \times 10^9/l$	Urine:	normal

Contd...

Contd...

ESR:	40 mm in 1st hour	ECG:	sinus tachycardia
Sodium:	136 mmol/l	Chest X-ray:	normal
Potassium:	3.4mmol/l		
Bicarbonate:	24 mmol/l		
Chloride	102 mmol/l		

QUESTIONS

- Q.1. What is the most likely diagnosis?
- Q.2. What further investigations would you ask for?
- Q.3. Name organisms responsible for this disease?
- Q.4. Name a few complications of this disease.
- Q.5. What is new about this disease?

ANSWERS

- A.1.** In this young man with a history of feeling cold then spiking temperature and followed by sweating with mild icterus suggests the diagnosis of malaria.
- A.2.** Blood film for malarial parasites is important. Both thick and thin films are recommended. Serological tests are also helpful in specification of the infecting organisms e.g., immunofluorescence, indirect haemagglutination and diffusion techniques ELISA for antigen detection and probes for parasite DNA are currently evaluated.
- A.3.** They are protozoa of the genus *Plasmodium*. There are four species which infect the human beings:
- i. *Plasmodium vivax*
 - ii. *Plasmodium ovale*
 - iii. *Plasmodium malariae*
 - iv. *Plasmodium falciparum*

Only female anopheles mosquito has proboscis which can pierce or puncture the skin to suck blood, whereas male mosquito has no proboscis, therefore, it cannot suck blood and transmit malaria.

- A.4.** These may be:
- i. Gross splenomegaly and potential rupture is common in *vivax* infections.
 - ii. Tropical splenomegaly syndrome.
 - iii. Cerebral malaria which may be fatal if not treated in time.
 - iv. Black-water fever due to massive intravascular haemolysis due to *falciparum* malaria.
- A.5.** Recent advances in malaria are:
- i. A synthetic vaccine SPf66 against *P. falciparum* has shown promising results in recent field trials. It is based on three merozoite-specific proteins (polypeptides) which are polymerised. Trials from Tanzania are encouraging.
 - ii Artemisinin which is derived from quinghaosu (a plant) has been widely used in China but rediscovered in 1979. It is parasitocidal against blood forms. It is less toxic and parasitic clearance and recovery from coma in

cerebral malaria is quicker than quinine. It is easy to administer. Results from Western trials are promising.

Oral = 50 mg tablet, Dosage given over 7 days—4 mg/kg 1st day then 2.0 mg/kg for day 2 and 3 then 1 mg/kg on days 4-7.

Injection = 60 mg/ampoule, Dosage: 1.2 mg/kg at 12 and 24 hours, then 1.2 mg/kg/day until the patient is fully conscious. On the day 4-7, 2.4 mg/kg/day IV or IM. (inj. is 60 mg which is diluted in 3-6 ml of 5% dextrose and is given as IV bolus).

DIAGNOSTIC MODALITIES FOR MALARIA

1. Light microscopy

This is a conventional method for diagnosing malaria. Giemsa stained thick and thin smears examined.

2. Fluorescent microscopy

Three fluorescent techniques for malaria diagnosis are available:

- i. Quantitative buffy-coat (QBC) method is the most well known.
- ii. Kawamoto Acridine-Orange procedure.
- iii. Bezo-thio Carboxy purine procedure.

3. Polymerase chain reaction based techniques

4. Antigen detection

Antigen capture test kits use a rapid, simple dipstick test from a finger prick blood sample to give a result in 10 to 15 minutes. This is called immunochromatographic test (ICT malaria Pf /Pv). It is sensitive as well as specific test.

Herpes Zoster

BRIEF HISTORY

A 50-year-old man presented to the accident and emergency department with a three-day history of rash on the right side of his cheek which was vesicular in nature and then it spreaded to the same side of the neck and back of it. There were associated symptoms of malaise and feeling of being unwell. He consulted local doctor who prescribed a cream for local application, but his condition deteriorated and he developed pustules. He also complained of swelling of his face and intolerable itching and pain in that area. He was a smoker and smoked 20 to 25 cigarettes per day. He was diabetic too and was taking tablets for it. He denied any use of chemical or soap on the face.

IMPORTANT CLUES ON CLINICAL EXAMINATION

On examination, a middle-aged chap who was distressed with pain. He had a nasty looking vesiculo-papular rash on the area of right cheek and jaw. A few vesicles were present on the same side of the neck. Some vesicles had turned into pustules. He had fever of 100°F and pulse was 98 per minute and regular with BP of 140/90 mmHg. Cardiovascular, respiratory and abdominal systems were normal. Nothing else was significant in neurological examination.

INVESTIGATIONS

Investigations revealed:

Hb :	13.4 g/dl (normocytic normochromic)	Chloride:	102 mmol/l
		Blood urea:	5.8 mmol/l (35 mg/dl)
		Creatinine:	138 umol/l (1.6 mg/dl)
WBC:	$12.6 \times 10^9/l$	Blood sugar:	10 mmol/l (180 mg/dl)
	P:78% L:18%	Urine:	normal except traces of albumin and sugar+++
	M:2% E:2%		

Contd...

Contd...

ESR:	32 mm in 1st hour	ECG:	normal
Sodium:	139 mmol/l	Chest X-ray:	normal
Potassium:	4.1 mmol/l		
Bicarbonate:	25 mmol/l		

QUESTIONS

- Q.1.** What is the most likely diagnosis?
- Q.2.** Where else can such a rash occur?
- Q.3.** What is the name given to the condition before the appearance of the rash?
- Q.4.** What are the complications of this disease?
- Q.5.** What is the treatment?

ANSWERS

- A.1. The most likely diagnosis in this middle-aged man who is a diabetic with a classical rash on his face is of *herpes zoster* of the trigeminal nerve. This is not very uncommon.
 - A.2. It can affect any part of the body, but it is common on trunk, sacral region, and rarely geniculate ganglion is involved resulting in ipsilateral Bell's palsy and vesicles in the external acoustic meatus called Ramsay Hunt syndrome.
 - A.3. If there is severe pain but no herpetic eruptions then it is called pre-herpetic neuralgia. It is very difficult to diagnose clinically but diagnosis can only be made if rising titres to varicella zoster virus are detected.
 - A.4. There may be superadded bacterial infection which is commonly due to *staphylococci*. Systemic spread may also occur. especially in immuno-compromised patients. Pupura fulminans is a rare complication and can cause too much tissue loss. Post-herpetic neuralgia is a very distressing and not uncommon complication which responds to 800 to 1200 mg of carbamazepine (Tegretol) per day in divided doses. Gabapentin (Neurositin) is an other option which can be given in a maximum dose of 1800 mg/day in divided doses. However, it is very expensive.
 - A.5. Early treatment with antiviral agents is worthwhile. Topical application of acyclovir (Zovirax) cream 5% or idoxuridine solution 40% has resulted in good effects). Systemic administration of antiviral agents, such as vidarabine 10 mg/kg/day and acyclovir 5-10 mg/kg 8 hourly have been recommended for herpetic involvement of maxillary and mandibular branch of trigeminal nerve, sacral zoster, purpura fulminans and encephalomyelitis. This results in very low incidence of post-herpetic neuralgia.

Interferon and hyperimmune globulins are also of value in systemic spread especially in immuno-compromised patients.
- NB:** Local application of acyclovir (Zovirax 5% cream) which is dermal preparation, rule of 5 is worth remembering, i.e. five percent cream, five times per day for five days.

BRIEF HISTORY

A 14-year-old girl presented to the medical outpatient department with a rash over her face, trunk and both upper and lower limbs for the last three days. Two days prior to the rash she developed fever of 101°F and consulted a local doctor and was given paracetamol. The fever subsided a little, but she developed irritation in her eyes and disliking for light. She had non-productive cough as well. She had no other physical illness and enjoyed a good health. One of her younger sisters had a feverish illness with a similar sort of rash about three weeks ago.

IMPORTANT CLUES ON CLINICAL EXAMINATION

On examination, she was pyrexial and temperature was 100.8°F. Her conjunctivae were mildly congested and there was a maculopapular rash which was of reddish brown in colour and had involved her face, forehead, neck, trunk and forearms. No vesicles were present. Her pulse was 88 per minute and regular. BP was 115/75 mmHg. Heart sounds were normal and chest was clear. Abdominal and neurological examinations were normal.

INVESTIGATIONS

Following investigations were asked:

Hb :	12.5 g/dl (normocytic normochromic)	Potassium:	3.9 mmol/l
		Bicarbonate:	25 mmol/l
		Chloride:	99 mmol/l
WCC:	$4.5 \times 10^9/l$ P: 76%, L: 18%, M: 4% E: 2%	Blood sugar:	4.0 mmol/l (72 mg/dl)
		Blood urea:	6.0 mmol/l (36 mg/dl)
		Creatinine:	82 umol/l (0.9 mg/dl)
Platelets:	$350 \times 10^9/l$	ESR:	18 mm in 1st hour
Sodium:	140 mmol/l		

QUESTIONS

- Q.1. What is the most likely diagnosis?
- Q.2. What is the pathognomonic lesion in this disease?
- Q.3. What is the causative agent?
- Q.4. List a few complications of this disorder.
- Q.5. How would you prevent this?

ANSWERS

- A.1.** In a young girl with a history of fever and flu-like illness following by a maculopapular rash in a classical distribution goes more in favour of an exanthem, i.e. measles.
- A.2.** These are called Koplik's spots and are small, irregular spots of bright red colour with a bluish white speck in the centre. They appear about 24 to 48 hours before the rash and are located in the buccal mucosa just at the level of the second upper molar tooth.
- A.3.** The causative agent is a virus which is a single stranded RNA virus. It exerts its cytopathic effect by developing multinucleated giant cell with inclusions in the nucleus and cytoplasm.
- A.4.** Different systems can be involved:
- Respiratory System*
- Acute laryngitis which may cause obstruction and even death.
 - Acute bronchiolitis, especially in younger children.
 - Lobar or bronchopneumonia due to superadded bacterial infection.
 - Pneumonitis due to immune deficiency.
- Nervous System*
- Short generalized seizures with complete recovery.
 - Measles encephalitis may be life-threatening and fatal. It is thought to be neuro-allergic phenomenon and not due to the direct invasion by the virus. If it is persistent, it can lead to subacute sclerosing panencephalitis (SSPE) which results in change of personality and behavioural disorders and ultimately results in signs of pyramidal and extra-pyramidal manifestation.
- Other complications of measles include haemorrhagic measles, thrombocytpaenia, paroxysmal cold haemoglobinuria, etc.
- A.5.** Passive immunization to the close contacts is important with human immunoglobulins if given within two to three days exposure. The usual dose is 0.2 ml/kg intramuscularly.

Currently, measles vaccine is used and is combined with mumps and rubella called MMR. It consists of live attenuated strains of viruses with low reactogenicity. The injection is given at 14 to 16 months of age. It is contra-indicated in pregnancy.

Digoxin Toxicity

BRIEF HISTORY

A man of 68 was admitted with a one-hour history of sudden severe chest pain radiating to his lower jaw with shortness of breath. He was sent to the ward after being given parenteral frusemide and diamorphine in the casualty department. He had occasional episodes of chest pain and dyspnoea on exertion in the past.

IMPORTANT CLUES ON CLINICAL EXAMINATION

On examination, he was found to be dyspnoeic and had central cyanosis. JVP was raised by four centimetres, but he had no ankle oedema, clubbing or lymphadenopathy. He had tripple rhythm and was fibrillating with an apical rate of one hundred and sixty per minute. He had diffuse bilateral basal crepitations with occasional rhonchi. Examinations of abdomen and central nervous system were normal.

Over the next two hours, his chest pain settled, but he was still in atrial fibrillation with fast ventricular response with a rate of about one hundred and fifty per minute. The house officer at this stage gave him a dose of 1 mg of digoxin parenterally and prescribed a further 0.25 mg. twice a day for the next forty-eight hours. After twenty-four hours, he was reported to have difficulty in differentiating the red from the green and blue and also complained of nausea and vomiting. His pulse rate at this stage was fifty eight per minute and irregular.

INVESTIGATIONS

Following were the results of various investigations:

Hb :	12.4 g/dl (normocytic normochromic)	Blood urea:	12 mmol/l (72 mg/dl)
		Creatinine:	138 μ mol/l (1.6 mg/dl)
WCC:	8.6×10^9 /l P: 70% L: 23% M: 5% E: 2%	Blood sugar:	7.4 mmol/l (133 mg/dl)
		Urine:	normal
Platelets:	260×10^9 /l	ECG:	atrial fibrillation with slow ventricular res- ponse and anterolateral ischaemic changes.
ESR:	14 mm in 1st hour		
Sodium:	136 mmol/l	Chest X-ray:	heart enlarged, bilateral pulmonary congestion.
Potassium:	3.4 mmol/l		
Bicarbonate:	24 mmol/l		
Chloride:	102 mmol/l		

QUESTIONS

- Q.1.** What is the most likely diagnosis?
- Q.2.** How would you confirm your diagnosis?
- Q.3.** Name four other drugs that may cause changes in colour vision.
- Q.4.** Name three other drugs which may be used for atrial fibrillation.

ANSWERS

- A.1.** The most likely diagnosis in this man is digoxin toxicity. Apart from the gastrointestinal (nausea and vomiting) and various cardiac dysrhythmias, digoxin may cause colour changes (red, green and blue defects), especially in the elderly. Classically, they have xanthopsia, i.e. yellow vision.
- A.2.** Serum digoxin levels if over 2.5 nmol/l would indicate digoxin toxicity.
- A.3.**
- Barbiturates.
 - Quinine and chloroquine.
 - Anti-epileptic drugs like tridione.
 - Anti-tubercular drugs like ethambutol.
- A.4.**
- Quinidine.
 - Verapamil.
 - Amiodarone.
- NB:** Digoxin toxicity should be treated as follows:
- Discontinue the drug.
 - Give potassium if hypokalaemia.
 - Administer atropine if severe bradycardia.
 - Temporary pacing.
 - Antibody fragment against digoxin which binds with digoxin called Digibind.

Phenytoin Toxicity

BRIEF HISTORY

A man of 72, known epileptic, was admitted with aches and bone pains all over the body and difficulty in climbing stairs for the last two months. He could not even get off a chair without support. His appetite was normal and there was no history of weight loss. There was no history of cough, chest pain or palpitations. He had a tendency towards constipation for many years but had only recently been started on Isophagol husk by his own doctor. His epilepsy had been well controlled with phenytoin 100 mg daily in the morning and 200 mg at night which he had been taking for the last one year. He was mostly house-bound and very occasionally used to go out.

IMPORTANT CLUES ON CLINICAL EXAMINATION

On examination, he was mentally alert. He looked pale and had marked kyphoscoliosis, but there was no clubbing, thyroid or lymph node enlargement. His BP was 140/95 mmHg and pulse was 80 per minute and regular. He had to be helped in getting out of a chair by two nurses and could walk only a step or two. Cardiovascular and respiratory systems were normal. He had some evidence of proximal muscle wasting in thighs, but the tone and reflexes were normal.

INVESTIGATIONS

Following investigations were performed:

Hb :	9.8 g/dl	Blood sugar:	7.2 mmol/l (129.6 mg/dl)
	(macrocytic	Creatinine:	140 umol/l (1.5 mg/dl)
	normochromic)	Bilirubin:	17 mmol/l (1.0 mg/dl)

Contd...

Contd...

MCV:	99 fl	Blood sugar:	7.2 mmol/l (129.6 mg/dl)
WCC:	8.2 × 10 ⁹ /l	Creatinine:	140 umol/l (1.5 mg/dl)
	P:82% L:16%	Bilirubin:	17 mmol/l (1.0 mg/dl)
	M:2% E:1%	Total protein:	6.4 g/l
Platelets:	300 × 10 ⁹ /l	Albumin:	3.4 g/dl
ESR:	40 mm in 1st hour	Alk Phos:	364 U/l
Sodium:	139 mmol/l	ALT:	30 U/l
Potassium:	3.7 mmol/l	Urine:	normal
Bicarbonate:	26 mmol/l	ECG:	normal sinus rhythm
Chloride:	100 mmol/l		with ventricular ectopics
Blood urea:	9.9 mmol/l	Chest X-ray:	normal
	(59 mg/dl)		

QUESTIONS

- Q.1. What is the most likely diagnosis, and why?
- Q.2. What else could be contributing to weakness in this patient?
- Q.3. What is the cause of his anaemia?
- Q.4. What other four investigations would you ask for in this patient?
- Q.5. What is the management?

ANSWERS

- A.1.** The most likely diagnosis in this aged patient is osteomalacia. Induction of liver enzyme resulting into excessive metabolism of 25-hydroxycholecalciferol is not uncommon in a patient who is on phenytoin for a prolonged period. So probably this is drug induced.
- A.2.** In house-bound elderly patient lack of exposure to sunlight and inadequate intake of vitamin D associated with poor nutrition are the factors which significantly contribute to his present state.
- A.3.** Macrocytic anaemia is one of the many side effects of phenytoin therapy. Poor nutritional status (low folate intake) may also be contributing towards anaemia.
- A.4.**
- i. Serum calcium and phosphorus.
 - ii. X-ray bones (scapulae and pelvis), to look for pseudo-fractures also called Looser's zones.
 - iii. Serum vitamin D level.
 - iv. Serum B₁₂ and folate levels.
- A.5.** Treatment is directed to the cause, if possible.
- i. For vitamin D deficiency, calciferol up to 2000-4000 i.u. daily is given with calcium supplements.
 - ii. Renal osteomalacia may be resistant and need 100,000 units daily, but serum calcium should be closely monitored.
 - iii. In glomerular failure, renal tubular acidosis must be corrected with bicarbonates, electrolytes and glucose.
 - iv. Diet plays an important role and its constituents should be proper.

Levodopa Toxicity

BRIEF HISTORY

A 65-year-old man was diagnosed to be suffering from parkinsonism and was started on levodopa increasing to 250 mg three times a day. Over the last few days, his rigidity and bradykinesia improved considerably with medicine, but unfortunately he started getting increased tremuors of his hands. He also became agitated and depressed and vomited on quite a few times. To control these symptoms effectively, he was given metoclopramide (maxolon) and diazepam. The sickness and agitational state improved, but he became more bedridden and lost interest in work and his routine also suffered. Nursing staff reported to the doctor the next day that he had been feeling rather low, complained of weakness and had asked for a particular tonic which had helped him three years ago. He was given some multivitamin tablets. However, his general condition deteriorated over the next few days and all that he wanted was to be left alone in bed and became more agitated if interfered with.

INVESTIGATIONS

Following were the results of various investigation at this stage:

Hb :	13 g/dl	Chloride:	102 mmol/l
	(normocytic	Blood urea:	9.9 mmol/l (59 mg/dl)
	normochromic	Creatinine:	140 umol/l (1.6 mg/dl)
WCC:	$9 \times 10^9/l$	Blood sugar:	7.1 mmol/l (128 mg/dl)
	P:82% L:16% M:2%	Urine:	normal
Platelets:	$300 \times 10^9/l$	ECG:	normal sinus rhythm
ESR:	34 mm in 1st hour		with ventricular ectopics
Sodium:	139 mmol/l	Chest X-ray:	normal
Potassium:	4.1 mmol/l		
Bicarbonate:	25 mmol/l		

QUESTIONS

- Q.1.** Why did the patient get increasing tremour on levodopa therapy?
- Q.2.** Why did the patient get worse on metoclopramide and diazepam?
- Q.3.** Name three other drugs which should be avoided, or used with care, in a patient on levodopa.
- Q.4.** What is off and on phenomenon?

ANSWERS

- A.1.** Levodopa is useful in relieving many of the symptoms of parkinsonism, particularly rigidity and bradykinesia. In many cases, it helps in controlling tremour but occasionally the tremour may get worse if too much levodopa is administered for a long time.
- A.2.** Metoclopramide is a dopamine antagonist and thus reduces the effect of levodopa. Diazepam and pyridoxine (in multivitamin tablets) are also known to have adverse drug interaction with levodopa reducing its effective blood levels.
- A.3.** i. Phenothiazines.
ii. MAO inhibitor—Type A.
iii. Phenytoin.
- A.4.** If the levodopa therapy is continued for a long time, then the patient becomes withdrawn or sometimes he is hyperactive. This stage usually occurs if the treatment has been given in high doses for many years.

Paracetamol Toxicity

BRIEF HISTORY

A young girl of 20 was admitted in the accident and emergency department with a history of ingestion of twenty-five tablets of paracetamol after a row with father, about ten hours ago. She started vomiting after a couple of hours and vomited a few tablets as told by the mother. She was a student at a college and was otherwise quite a jolly girl.

IMPORTANT CLUES ON CLINICAL EXAMINATION

On examination, she was a bit restless. Pallor was obvious. Pulse was 88 per minute and regular. BP was 110/70 mmHg. She was tender in the epigastrium, but respiratory and cardiovascular examinations were normal. She responded to verbal commands. No other focal neurological signs were present.

INVESTIGATIONS

Following investigations were performed:

Hb :	12.2 g/dl	Potassium:	4.6 mmol/l
	(normocytic	Bicarbonate:	25 mmol/l
	normochromic)	Chloride:	99 mmol/l
WCC	$6.4 \times 10^9/l$	Blood glucose	4.6 mmol/l (83 mg/dl)
	P:70, L:24%,	Blood urea	6.0 mmol/l (36 mg/l)
	M:3%, E:3%	Creatinine	110 umol/l (1.2 mg/dl)
Platelets:	$320 \times 10^9/l$	Urine:	normal
ESR:	10 mm in 1st hour		
Sodium:	136 mmol/l		

She was given some treatment but next day she became confused and restless and started bleeding from nose. Her urine output also decreased.

IMPORTANT CLUES ON REPEATED CLINICAL EXAMINATION

On examination, there was mild tinge of jaundice but she was tender in the right hypochondrium and flapping tremours were present, too.

Liver function test showed:

Bilirubin :	22 umol/l (1 mg/dl)
SGOT :	2350 U/l
SGPT :	3282 U/l
Alk. phos. :	237 U/l

QUESTIONS

- Q.1.** What happened on the second day?
- Q.2.** What is the lethal dose of acetaminophen?
- Q.3.** What most important investigation should be asked straightway after such an overdose?

ANSWERS

- A.1.** Paracetamol or acetaminophen poisoning is notorious to cause hepatic damage after 24 to 48 hours, but it depends on individual variations. These are metabolites of acetaminophen and not the drug itself. The serum transaminases may rise quite high and even severe hepatic necrosis can occur causing death.
- A.2.** This varies from patient to patient. However, hepatic damage may be anticipated if an adult has taken more than 8 grams (16 tablets) as a single dose.
- A.3.** Acetaminophen levels in plasma—it is very important. A plasma concentration of greater than 200 ug /ml at four hours after ingestion is of great concern. After 16 hours administration of Parvolex (Acetylcysteine-antidote) is not recommended.

Treatment is most effective if started between 8 to 10 hours after ingestion of paracetamol.

*Hypothermia***BRIEF HISTORY**

A man in his early seventies was brought to the accident and emergency department after a fall. He was unable to get up from the floor. His family members after coming from a wedding found him on the floor and it was not quite certain for how long he had been like that. History from the relatives revealed that he had been complaining of pain in his both knees, poor mobility and had recently been started on some antidepressant tablets along with the painkillers by a general practitioner.

IMPORTANT CLUES ON CLINICAL EXAMINATION

On examination, he was confused and disorientated. His skin was cold and clammy with peripheral cyanosis. Temperature was 91.4°F in axilla and 92.1°F rectally. There was no clubbing or lymphadenopathy. He had marked osteoarthritis of his knees. Blood pressure was 100/60 mmHg and pulse was 64 per minute. Respiratory, cardiovascular and abdominal examinations were normal. Cranial nerves were intact and there were no localising neurological signs.

INVESTIGATIONS

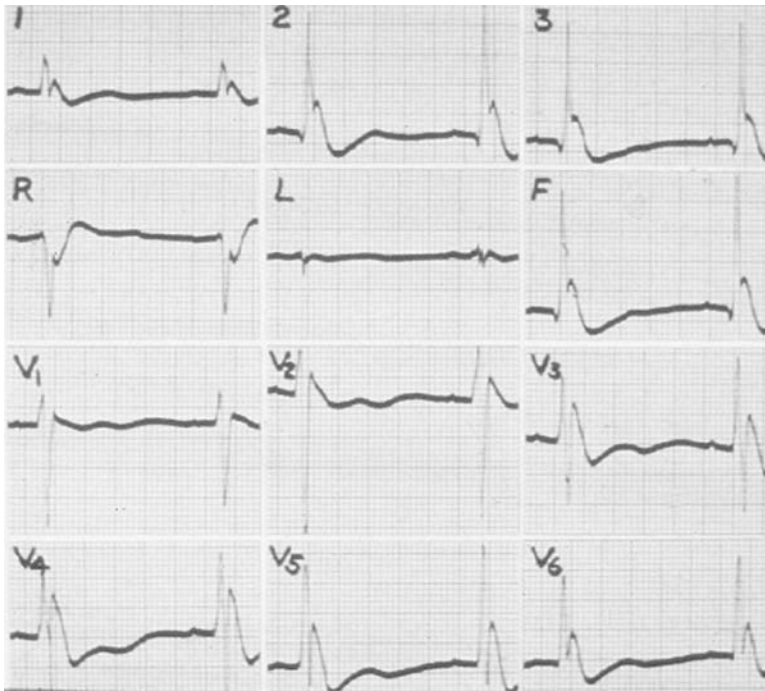
Following were the results of various investigations:

Hb :	14.2 g/dl	Chloride:	100 mmol/l
	(normocytic	Blood sugar:	7.1 mmol/l (128 mg/dl)
	normochromic)	Blood urea:	12 mmol/l (72 mg/dl)
WCC:	$9.2 \times 10^9/l$	Creatinine:	156 umol/l (1.8 mg/dl)
	P:74% L:22%	Urine:	normal
	M:2% E:2%	ECG:	as shown in Figure 91.1

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Platelets:	230 × 10 ⁹ /l	Chest X-ray:	no lung lesion, heart size normal
ESR:	42 mm in 1st hour		
Sodium:	143 mmol/l		
Potassium:	4 mmol/l		
Bicarbonate:	20 mmol/l		

**Fig. 91.1****QUESTIONS**

- Q.1. What is the diagnosis?
- Q.2. Describe the ECG.
- Q.3. Name four other drugs which may be contributing to this diagnosis.
- Q.4. Why is rapid rewarming not recommended?
- Q.5. List four other complications of this condition.

ANSWERS

- A.1.** The diagnosis in this elderly gentleman with low axillary and rectal temperature is obviously hypothermia. His fall may have been due to poor mobility with osteo-arthritis of his knees and hips. Further, postural hypotension is a common side effect of antidepressants in the elderly and may have contributed to his fall. Confusion is consistent with the diagnosis of hypothermia but may also result from depression (pseudodementia) and antidepressant therapy. Hypothermia in the elderly usually results from a faulty temperature regulatory mechanism and may be coupled with one or more systemic illnesses or drug therapy such as with antidepressants.
- A.2.** It shows sinus bradycardia with junctional 'J' waves after QRS complexes which is classical of hypothermia.
- A.3.**
- i. Phenothiazine
 - ii. Barbiturates
 - iii. Anticholinergic drugs
 - iv. Benzodiazepines
- A.4.** Extensive cutaneous vasodilatation associated with rapid rewarming may result in falling arterial blood pressure and inadequate coronary perfusion. In some cases, the vasodilatation allows less blood to reach the body core, thus, causing a further fall in core temperature.
- A.5.**
- i. Acute pancreatitis
 - ii. Severe hypoglycaemia
 - iii. Metabolic acidosis
 - iv. Ventricular fibrillation and death.

BRIEF HISTORY

A 26-year-old woman attended the accident and emergency department with sudden onset of central abdominal pain and vomiting. The pain radiated to the back as well. Simultaneously, she felt that lower limbs were weak and also complained of difficulty in breathing. There was a history of sweating, palpitations and headaches. Her menstrual history was unremarkable but she did mention about the passage of dark urine which turned even darker if left for a short time. No family history was traceable.

IMPORTANT CLUES ON CLINICAL EXAMINATION

On examination, she was in distress. Her pulse was 128 per minute and regular while her blood pressure was 140/100 mmHg. She had a temperature of 99°F. Cardiovascular system was normal. The bowel sounds were present and there was a succussion splash. Neurological examination showed weak tendon reflexes and derranged sensations of touch and pain.

INVESTIGATIONS

Following investigations were performed:

Hb :	13.4 g/dl	Blood Sugar:	6 mmol/l (108 mg/dl)
	(normocytic	Blood urea:	13 mmol/l (78 mg/dl)
	normochromic)	Creatinine:	138 umol/l (1.6 mg/dl)
WCC:	$14.2 \times 10^9/l$	Bilirubin:	44 umol/l (2.6 mg/dl)
	P:74% L:22%	SGOT:	120 U/l
	M:2% E:2%	SGPT:	240U/l
Platelets:	$290 \times 10^9/l$	Urine:	normal

Contd...

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ESR:	45 mm in 1st hour	ECG:	sinus tachycardia
Sodium:	138 mmol/l	Chest X-ray:	normal
Potassium:	3.8 mmol/l		
Bicarbonate:	24 mmol/l		
Chloride:	99 mmol/l		

QUESTIONS

- Q.1.** What is the most likely diagnosis?
- Q.2.** List a few more investigations.
- Q.3.** What is the management?

ANSWERS

A.1. In a young female with a history of abdominal pain, paraesthesia, weakness and passage of dark urine which turns even darker on standing favours a diagnosis of acute intermittent porphyria.

A.2. These include:

- i. Demonstration of excess porphobilinogen in the urine (PBG). Normal : 0-3.6 mg/day.
- ii. Raised urinary δ -amino laevulinic acid (ALA). Normal: 0-5.3 mg/day.
- iii. Raised urinary uroporphyrins. Normal: 0-41 ug/day.
- iv. Raised urinary coproporphyrin. Normal: 0-280 ug/day.

A.3. Acute attack carries a significant mortality. Early diagnosis, removal of precipitating factors and provision of intensive supportive therapy. Administration of haem may speed up recovery.

Important aspects to remember are:

- i. *Nutrition* Adequate carbohydrate intake should be ensured. Two litres of 25 percent dextrose should be infused every 24 hours via central line.
- ii. *Analgesia* Pethidine or diamorphine may be required, but risk of narcotic addiction should be kept in mind.
- iii. *Tachycardia and hypertension* These should be controlled with beta blockers and large dose is required. Pulse and blood pressure should be closely monitored.
- iv. *Convulsions* These may be secondary to hyponatraemia due to SIADH secretion. Management of chronic epilepsy in porphyric patients is extremely difficult.
- v. *Neuropathy* If respiratory embarrassment occurs, blood gases should be checked and patient should be nursed in intensive care unit with ventilatory facilities. Appropriate physiotherapy is required.
- vi. *Haematin therapy* This reduces overproduction of porphyrins by suppressing the activity of the initial enzymatic pathway of δ -amino laevulinic acid synthase. It is administered in a dose of 3 mg/kg/day iv over 15 minutes for three to four days. It should be avoided in patients with coagulopathy. Recent studies have demonstrated that the biochemical remission

induced by haematin therapy can be prolonged by co-administration of tin-protoporphyrin which inhibits the break down of haem by haem oxygenase. Skin photo sensitivity should be avoided.

NB: Various factors may precipitate acute attack with the genetic trait.

These are:

1. Drugs
2. Alcohol
3. Fasting
4. Hormones
5. Infections.

There is a long list of medications which are unsafe to be used in this condition.

Attacks should be prevented and the doctor must know the history of the patient. Some women experience regular attacks in the week prior to the onset of menstruation. Pregnancy may precipitate acute attack of porphyria. This is very important to remember that due to abdominal pain even laparotomies have been carried out, therefore, acute porphyria should be ruled out.

Toxic Shock Syndrome

BRIEF HISTORY

A 26-year-old woman was admitted through accident and emergency department with a two-day history of high grade fever and diarrhoea along with vomiting and myalgia. There was history of vaginal discharge which was not itchy but was purulent. There was no history of any upper or lower respiratory tract infection. She belonged to a lower class family, was married and had one child. Her menstrual cycle finished three days prior to her admission in the hospital and she used tampons for this. She also complained of peeling of skin from her hands and feet. There was no other relevant history from the patient.

IMPORTANT CLUES ON CLINICAL EXAMINATION

On examination, she looked exhausted, sweaty and very anxious. Her temperature was 104°F and pulse was 130 per minute and regular. Her blood pressure was recorded at 85/60 mmHg. Heart sounds were normal. Respiratory and abdominal examinations were normal. Neurologically, she was confused and drowsy, but there were no signs of meningeal irritation. However, there were patches of desquamation on hands and feet.

INVESTIGATIONS

Following investigations were asked:

Hb :	12.6 g/dl	Blood Sugar:	5.5 mmol/l (99 mg/dl)
	(normocytic	Blood urea:	10 mmol/l (60 mg/dl)
	normochromic)	Creatinine:	100 umol/l (1.1 mg/dl)
WCC:	$23.5 \times 10^9/l$	Blood cultures:	no growth obtained
	P:84% L:12%	after 24 hours	
	M:2% E:2%	Urine:	normal

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Platelets:	170 × 10 ⁹ /l	ECG:	sinus tachycardia, no
ESR:	68 mm in 1st hour		evidence of ischaemia
Sodium:	138 mmol/l	Chest X-ray:	normal.
Potassium:	3.4 mmol/l		
Bicarbonate:	24 mmol/l		
Chloride:	99 mmol/l		

QUESTIONS

- Q.1.** What is the most likely diagnosis?
- Q.2.** What further two investigations are required?
- Q.3.** Discuss the management.

ANSWERS

- A.1.** In a female of reproductive age who developed high-grade fever with rapid deterioration in her condition and history of using tampons for menstrual blood along with desquamation of hands and feet favours the most likely diagnosis of toxic shock syndrome (TSS).
- A.2.**
- Vaginal swab for isolation of *staphylococcus aureus* (Gram stain) phage group I and lysed by phage 29 or 52.
 - Isolation of antitoxic shock syndrome toxin (TSST-I) antibodies from serum.

NB: Blood cultures are usually negative.

- A.3.** The management is mainly supportive and includes to correct shock. Anti-staphylococcal antibiotics should be given to eradicate *S. aureus* from the local site (vagina) and any tampons should be removed immediately.

Various antibiotics can be used to eradicate the toxin producing *S. aureus*. B-lactamase resistant penicillins, e.g. flucloxacillin or cephalosporins are appropriate. Others included in the list are methicillin, cloxacillin, dicloxacillin, oxacillin, nafcillin and augmentin. Third-generation cephalosporins are less active against *S. aureus*. If a patient is hypersensitive to penicillin, then macrolides, e.g. erythromycin and orclarithromycin are good alternatives. Fusidic acid is an excellent anti-staphylococcal agent.

Goodpasture's Syndrome

BRIEF HISTORY

A 34-year-old male was admitted in the medical ward with a three days history of upper respiratory tract infection followed by cough, which was dry to start with but later on became mildly purulent. Two days later he noticed pure blood in the sputum. There was low grade fever all the time inspite of a course of antibiotics. No positive family history was traceable. He smoked 10-12 cigarettes a day.

IMPORTANT CLUES ON CLINICAL EXAMINATION

On examination, he looked pale. Pulse was 100 per minute and regular. Blood pressure was 140/95 mmHg. Throat was congested. His temperature was 99.4°F. Chest revealed few crackles bilaterally. Heart sounds were normal. Abdominal and neurological examinations were unremarkable. He improved with symptomatic treatment, but three weeks later again presented with dark coloured urine, swelling of feet and face and frothy urine which was of dark colour.

INVESTIGATIONS

Following investigations were performed:

Hb:	9.2 g/dl (normocytic normochromic)	Blood sugar:	6 mmol/l (108 mg/dl)
		Blood urea:	12 mmol/l (67 mg/dl)
		Creatinine:	150 umol/l (1.7 mg/dl)
WCC:	$10.2 \times 10^9/l$	Urine:	protein++, blood++
	P:76% L:20% M:2% E:2%	ECG:	sinus tachycardia, no evidence of ischaemia

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Platelets:	$278 \times 10^9/l$	Chest X-ray:	normal cardiac size,
ESR:	79 mm in 1st hour		diffuse infiltrations in the
Sodium:	138 mmol/l		lungs and small right-
Potassium:	5.2 mmol/l		sided pleural effusion
Bicarbonate:	24 mmol/l		
Chloride	99 mmol/l		

QUESTIONS

- Q.1. What is the most likely diagnosis?
- Q.2. What is aetiology?
- Q.3. What two further investigations would you require?
- Q.4. Discuss the management.

ANSWERS

- A.1.** In a patient with upper respiratory tract infection, haemoptysis and after a few weeks followed by haematuria, proteinuria and blotchy appearance on chest X-ray favours a diagnosis of Goodpasture's syndrome.
- A.2.** It is thought to be due to type II cytotoxic hypersensitivity reaction. The hypothesis is that there may be a shared antigen between a virus and the basement membrane of both kidneys and lungs.
- A.3.** These are:
- i. Anti-glomerular basement membrane (anti-GBM) antibodies in the serum.
 - ii. Raised plasma anti-neutrophilic cytoplasmic antibodies (ANCA).
- A.4.** The treatment consists of:
- i. Corticosteroids
 - ii. Plasmapheresis
 - iii. Supportive management for both lung and kidney involvement.
- NB:** When oliguria occurs or serum creatinine rises above 6 to 8 mg/dl, renal failure is almost irreversible.

Milroy's Disease

BRIEF HISTORY

A 62-year-old lady was referred to the medical outpatient for assessment for her leg oedema and painful knees. She recently had noticed excessive thirst and was passing urine more frequently at night. She also complained of aching legs and easy fatigueability. She denied any history of chest pain, palpitations, cough or expectoration. She had not been taking any drugs apart from occasional paracetamol.

IMPORTANT CLUES ON CLINICAL EXAMINATION

On questioning, it was revealed that the legs had been oedematous for the last forty years and her sister who died four years ago had a similar problem, i.e. swollen legs. On examination she was obese, mentally alert and cheerful. JVP was not raised. She had bilateral non-pitting oedema of her legs. Blood pressure 140/70 mmHg, pulse eighty per minute regular. There was no clubbing, jaundice, thyroid or lymph node enlargement. She was in sinus rhythm with no heart murmur. Respiratory and nervous system examinations were normal. Apart from osteoarthritis of both knees, other joints were clinically normal with good range of movements.

INVESTIGATIONS

Following were the results of various investigations:

Hb :	14.1 g/dl (normocytic normochromic)	Chloride:	100 mmol/l
		Blood urea:	10.0 mmol/l (60 mg/dl)
		Creatinine:	135 μ mol/l (1.5 mg/dl)
WCC:	8×10^9 /l	Blood sugar:	11.9 mmol/l (214 mg/dl)
	P:72% L:24%	Urine:	sugar++, no albumin
	M:2% E:1%	ECG:	normal sinus rhythm,

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ESR:	21 mm in 1st hour	no ischaemic changes.
Sodium:	139 mmol/l	Chest X-ray: normal
Potassium:	4.1mmol/l	
Bicarbonate:	22 mmol/l	

QUESTIONS

- Q.1.** What is the most likely diagnosis?
- Q.2.** What is the basic pathology in this disease?
- Q.3.** What is the mode of transmission of this disease?
- Q.4.** Give three causes of secondary lymphoedema.
- Q.5.** What treatment can be offered?

ANSWERS

- A.1.** The most likely diagnosis in this lady with long standing non-pitting oedema of both legs and family history of similar disorder with no evidence of heart failure is Milroy's disease. The aetiology is probably congenital malformation of lymphatic channels. Besides Milroy's disease she has late onset diabetes and osteoarthritis of the knees.
- A.2.** There is agenesis of subcutaneous lymphatic vessels in this disease.
- A.3.** The mode of inheritance is thought to be autosomal dominant.
- A.4.**
- i. Invasion of lymph nodes by carcinomatosis.
 - ii. Surgical removal of lymph nodes, e.g. in radical mastectomy.
 - iii. Recurrent lymphangitis, e.g. filariasis common in tropics resulting in elephantiasis.
- A.5.** Surgical treatment can be offered. It involves attempting to establish lymphatic flow by "swiss roll" procedure. However, this may result in mild improvement.

BRIEF HISTORY

A 70-year-old lady was admitted via accident and emergency department with a three-month history of frequent falls. During the week before her admission, she had two falls. Both occurred at home and without any prior warning and were not associated with loss of consciousness. She denied having any chest pain, but did admit to fluttering in the chest and giddiness lasting for a minute or so before the falls. She had previously been fit and had not been taking any drugs. Even at this age, she was quite independent and enjoyed good health.

IMPORTANT CLUES ON CLINICAL EXAMINATION

On examination, she was mentally alert. Blood pressure was 140/80 mmHg while sitting, 135/70 mmHg while standing. There was no anaemia, clubbing or tremour. JVP was not raised. Examination of the joints was normal, in particular her neck movements were full without any associated giddiness and pain. There were no carotid bruits. She was in sinus rhythm and had no heart murmur. Examinations of respiratory and neurological systems were normal and so was the abdominal examination.

INVESTIGATIONS

Following were the results of various investigations:

Hb :	13 g/dl (normocytic normochromic)	Chloride:	101 mmol/l
		Creatinine	143 umol/l (1.6 mg/dl)
		Blood sugar:	7.4 mmol/l (133 mg/dl)
WCC:	$8 \times 10^9/l$	Bilirubin:	17 umol/l (1.0 mg/dl)
	P:71% L:26%	Total proteins:	6.2 g/dl
	M:2% E:1%	Albumin:	3.3 g/dl

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Platelets:	300 × 10 ⁹ /l	Urine:	normal
ESR:	29 mm in 1st hour	ECG:	anterolateral ischaemic changes with occasional supraventricular and ventricular ectopics.
Sodium:	140 mmol/l		
Potassium:	3.4 mmol/l		
Bicarbonate:	28 mmol/l		
Chloride:	102 mmol/l	Chest X-ray:	unfolding of the aorta, no cardiomegaly, lung fields were clear.
Blood urea:	6.7 mmol/l (40 mg/dl)		

QUESTIONS

- Q.1.** Give five cardiovascular causes of falls in the elderly.
- Q.2.** Considering the ECG findings would you ask any more investigation?
- Q.3.** How would you manage the patient described above?
- Q.4.** What are drop attacks?
- Q.5.** What rare causes should be kept in mind in this regard?

ANSWERS

- A.1.** i. Postural hypotension.
ii. Cardiac dysrrhythmia (heart blocks, bradycardia, tachycardia).
iii. Transient ischaemic attacks (vertebrobasilar insufficiency).
iv. Aortic stenosis (syncopal attacks).
v. Myocardial infarction (causes hypotension which may lead to shock).
- A.2.** Yes, 24 hours Holter monitoring (Medlog) to know the rhythm and rule out any periods of sinus arrest, tachycardia or bradycardia and sick sinus syndrome.
- A.3.** This patient probably has a sick sinus syndrome causing tachy-brady-arrhythmia. A permanent pacemaker is indicated in such situations.
- A.4.** Drop attacks are characterised by sudden falls without any warning or loss of consciousness. For some unknown reasons, drop attacks are almost always seen in middle-aged or elderly women. Falls occur only on walking rather than standing and they often happen in the street and not indoors. The aetiology of drop attacks is far from being clear. In some patients, at least they are thought to be associated with vertebrobasilar insufficiency. Concomitant severe anaemia aggravates symptoms.
- A.5.** Whether due to hysterical hyperventilation or due to low serum calcium, tetany should be kept in mind. Narcolepsy and cataplexy must not be forgotten either.

BRIEF HISTORY

A 71-year-old man was admitted with a history of poor general health, increased tiredness and excessive bruising over his lower limbs. There was no history of trauma, cough, expectoration, chest pain or palpitation. His appetite had not changed recently but he admitted that he was never a big eater. There was no history of loss of weight. He had not been taking any drugs. He belonged to a poor socio-economic class and was living just from hand to mouth. He hardly took any fresh fruits or vegetables.

IMPORTANT CLUES ON CLINICAL EXAMINATION

On examination, he was pale, apathetic and edentulous. Blood pressure was 140/70 mmHg and pulse was eighty eight per minute and regular. JVP was not raised. There was no clubbing, thyroid or lymph node enlargement. He had extensive perifollicular haemorrhages over his thighs and buttocks. Petechial haemorrhages and purpuric spots were also noted on both legs and feet. Examination of cardiovascular, respiratory, gastrointestinal and neurological system was unremarkable.

INVESTIGATIONS

Following were the results of various investigations:

Hb :	10.2 g/dl (normocytic normochromic)	Bicarbonate:	24 mmol/l
		Chloride:	96 mmol/l
WCC:	$8 \times 10^9/l$	Blood urea:	9.9 mmol/l (59 mg/dl)
	P:72% L:25%	Creatinine:	135 μ mol/l (1.5 mg/dl)
	M:2% E:1%	Blood sugar:	8 mmol/l (144 mg/dl)
		Urine:	normal

Contd...

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Platelets:	$256 \times 10^9/l$	ECG:	normal sinus rhythm
Prothrombin		Chest X-ray:	normal
time:	normal		
ESR:	24 mm in 1st hour		
Sodium:	138 mmol/l		
Potassium:	4.1 mmol/l		

QUESTIONS

- Q.1.** What is the most likely diagnosis?
- Q.2.** Give two investigations which help the diagnosis.
- Q.3.** Give five complications of this disease.
- Q.4.** What is scorbutic rosary?
- Q.5.** How would you manage such a patient?

ANSWERS

- A.1.** The most likely diagnosis in this elderly man with anaemia, perifollicular and petechial haemorrhages on his thighs and legs with normal platelet count and prothrombin time is scurvy.
- A.2.**
- i. Estimation of platelet ascorbic acid level. Usually less than a fourth of the normal (52 ± 22 micro gram/ 10^{10} platelets.)
 - ii. Estimation of urinary excretion of vitamin C after a "loading" dose of vitamin C.
- A.3.**
- i. Extensive haemorrhages and haemarthrosis.
 - ii. Slow wound healing.
 - iii. Delayed or non-union of fractures.
 - iv. Accelerated osteoporosis.
 - v. Sudden death.
- A.4.** In infancy due to vitamin C deficiency, the sternum may sink inwardly, leaving a sharp elevation at the rib margin called scorbutic rosary.
- A.5.** Scurvy is potentially fatal and treatment should never be delayed. Usual regimen is 100 mg three to four times a day until 4 grams have been administered. Afterwards it is 100 mg per day. A diet rich in vitamin C should be administered.

Carcinoid Syndrome

BRIEF HISTORY

A 38-year-old man presented to the medical outpatient department with a six-month history of flushing over face and neck. This used to be accompanied by a feeling of heart sinking and palpitations. He also mentioned about passing loose motions and had developed generalized weakness. A couple of months ago, he had severe breathlessness and was admitted in the hospital for asthma. There was no history of any drug intake and no one else in the family was suffering from such symptoms.

IMPORTANT CLUES ON CLINICAL EXAMINATION

On examination, he had telangiectasia on his face. Pulse was 110 per minute and regular. JVP was up to 3 cm and BP was 120/75 mmHg. Heart sounds were normal, but there was a systolic murmur at pulmonary area. Chest examination revealed bibasal crackles and occasional wheezing. Gastrointestinal and neurological systems were unremarkable.

INVESTIGATIONS

Following investigations were performed.

Hb :	13.4 g/dl (normocytic normochromic)	Blood urea:	6.2 mmol/l (37 mg/l)
		Creatinine:	100 umol/l (1.1 mg/dl)
		Urine:	normal
WCC	$9.7 \times 10^9/l$ P: 72% L: 26%, M: 1%, E: 1%	Chest X-ray:	heart size within normal limits.
Platelets:	$320 \times 10^9/l$	ECG:	right axis deviation with incomplete right bundle

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ESR:	12 mm in 1st hour	branch block, tall peaked
Sodium:	138 mmol/l	P waves were noticed
Potassium:	4.1 mmol/l	in lead II.
Bicarbonate:	25 mmol/l	
Chloride:	99 mmol/l	

QUESTIONS

- Q.1.** What is the most probable diagnosis?
- Q.2.** What is the most important investigation in this disorder?
- Q.3.** What is the mechanism of flushing in this disorder?
- Q.4.** What treatment can be offered?

ANSWERS

- A.1.** In a middle-aged man with history of flushing and wheezing and clinical presence of telangiectasia on the face with pulmonary stenosis and ECG evidence of pulmonary hypertension indicate a diagnosis of carcinoid syndrome.
- A.2.** Excretion of 5-hydroxy indole acetic acid (5-HIAA) is increased in the urine in 24 hours. A reading more than 9 mg/day is diagnostic. However, it is a sensitive test and false positive results may be obtained after ingestion of bananas, walnuts, phenothiazines and cough syrups containing guaiacolate.

Measurement of serotonin in blood or platelets is of interest but it has less diagnostic value.

- A.3.** Many chemical mediators are involved in the production of flushing in carcinoid syndrome including histamines. Release of the flush-provoking substances can be triggered by catecholamines which explain flushing after excitement and emotional stimuli. Others include serotonin and bradykinines.
- A.4.** Complete cure with surgery is possible after detection of localized carcinoid.

Chemotherapy is directed against humoural mediators. Combination therapy of H_1 and H_2 antagonists in gastric carcinoid may be helpful.

Methysergide, a serotonin antagonist will improve the diarrhoea, but prolonged therapy with this drug may produce retroperitoneal fibrosis.

Blockade of serotonin synthesis with chlorophenylalanine will also help stopping diarrhoea. Corticosteroids may also help preventing flushing.

If hypotension requires therapy, volume expansion or methoxamine infusion is a preferred approach.

BRIEF HISTORY

A 53-year-old gentleman was seen in the outpatient department with a two-year history of painful shoulder joints and left knee joint. He also complained that the neck movements were painful and the pain was shooting in character radiating to both arms. There was no history of involvement of the small joints of hands. He himself mentioned that when he passed urine, it became dark and that had been like this since his childhood, but he never took any notice of that. In the past, he had a cerebrovascular accident from which he recovered fully.

He was suffering from diabetes mellitus and ischaemic heart disease and was on appropriate medications. There was no positive clue in the family history.

IMPORTANT CLUES ON CLINICAL EXAMINATION

On examination, he was in obvious distress due to pain in left shoulder. General physical examination was normal. BP was 120/80 mmHg and pulse was 84 per minute and regular. Cardiovascular, respiratory, abdominal and neurological systems were unremarkable. Examination of the left shoulder revealed painful movements in all directions and crepitus in the joint was noticed. There was obvious wasting of the muscles around left shoulder.

INVESTIGATIONS

Following investigations were performed.

Hb :	12.2 g/dl	Bicarbonate:	25 mmol/l
	(normocytic	Chloride:	101 mmol/l
	normochromic)	Blood urea:	5.2 mmol/l (31 mg/l)

Contd...

Contd...

WCC	9.2 × 10 ⁹ /l	Creatinine:	87 umol/l (0.9 mg/l)
	P: 70% L: 28%	Urine:	normal
	M: 1% E: 1%	X-ray left	degenerative changes
Platelets:	300 × 10 ⁹ /l	shoulder:	with narrowing of joint
ESR:	22 mm in 1st hour		space
Sodium:	136 mmol/l		
Potassium:	3.9 mmol/l		

QUESTIONS

- Q.1.** What is the most likely diagnosis?
- Q.2.** How would you diagnose this condition?
- Q.3.** Name few tests by which this condition can be identified.
- Q.4.** What is the incidence and mode of inheritance?
- Q.5.** What is the treatment?
- Q.6.** Name few causes of dark urine.

ANSWERS

- A.1.** In a patient who has generalized arthritis but affecting his few joints badly and a long history of passing urine which turns dark on standing goes in favour of alkaptonuria (ochronosis).
- A.2.** The diagnosis is made from a triad:
- i. Degenerative arthritis
 - ii. Ochronotic pigmentation
 - iii. Urine which turns black on alkalinization.
- A.3.** These include:
- i. If ferric chloride is added to urine, a purple colour is formed.
 - ii. If treated with Benedict's reagent, a brown colour is obtained.
 - iii. Addition of saturated silver nitrate solution gives a black colour immediately.
 - iv. Chromatography.
 - v. Enzymatic assay.
 - vi. Spectrophotometric analysis.
- A.4.** It is present in one in 200,000 and is carried as autosomal recessive trait. There is deficiency of enzyme homogentisic acid oxidase.
- A.5.** There is no treatment as such. However, dietary restriction of phenylalanine and tyrosine is recommended. Use of vitamin C due to its anti-oxidation and anti-polymerization property may decrease pigment formation and deposition in the joints.
- A.6.** These include:
- i. Alkaptonuria
 - ii. Black water fever
 - iii. Drugs, e.g. phenolphthaline and rifampicin
 - iv. Beetrooturia
 - v. Haematuria
 - vi. Obstructive jaundice
 - vii. Highly-concentrated urine.

Malignant Melanoma

BRIEF HISTORY

A man of 56 was admitted with a four-month history of weight loss of more than 6 kg. He also had poor appetite, generalised weakness and poor mobility. There was no history of cough or expectoration, chest pain, palpitation, and urinary or bowel symptoms. About 18 months ago, he had his right eye enucleated and apart from this enucleated eye he had always been fit and healthy. There was no history of hypertension or diabetes mellitus.

IMPORTANT CLUES ON CLINICAL EXAMINATION

On examination, he was pale and wasted. There was no clubbing, oedema or lymphadenopathy. Blood pressure was 140/70 mmHg. Pulse was 80 per minute and regular. His skin was normal. There were no spider naevi, Dupuytren's contracture or palmar erythema. Examinations of cardiovascular and respiratory systems were normal. His liver was 6 cm enlarged, hard, nodular with an irregular surface and was tender. Spleen was not palpable and there was no ascites. Rectal examination and proctoscopy were normal. There were no significant findings in the nervous system apart from the right enucleated eye in which he had an artificial implant.

INVESTIGATIONS

Following results were available:

Hb :	8.4 g/dl (normocytic normochromic)	Potassium :	3.4 mmol/l
		Bicarbonate:	24 mmol/l
		Chloride:	100 mmol/l
WCC:	$10 \times 10^9/l$	Blood urea:	8.9 mmol/l (53 mg/l)

Contd...

Contd...

	P: 79% L: 18%	Blood sugar: 6.4 mmol/l (115 mg/dl)
	M: 2% E: 1%	ECG: normal sinus rhythm
ESR:	25 mm in 1st hour	
Sodium:	134 mmol/l	

QUESTIONS

- Q.1.** What is the most likely diagnosis?
- Q.2.** What three investigations will you ask for?
- Q.3.** Give four other sites commonly involved by this condition.
- Q.4.** What are the features that indicate that a benign naevus has changed to a malignant lesion?

ANSWERS

- A.1.** The most likely diagnosis in this man with previous enucleation of eye, poor appetite, significant weight loss, cachexia and hepatomegaly is malignant melanoma with liver metastases. Hard, irregular, nodular and tender liver is always suggestive of metastases and in this case the primary was more than likely in the enucleated eye.
- A.2.**
- i. Liver function tests
 - ii. Abdominal ultrasound
 - iii. Liver biopsy.
- A.3.**
- i. Nails of fingers, and toes.
 - ii. Anus.
 - iii. Nose, mouth.
 - iv. Skin.
- A.4.** These are:
- i. Increase in the intensity of pigmentation.
 - ii. Itching.
 - iii. Bleeding.
 - iv. Ulceration.
 - v. Deep invasion of the tumour to the surrounding tissues.
 - vi. Loss of hair from a hairy naevus.
- NB:** One must remember ABCD about malignant melanoma. "A" stands for asymmetry of lesion. "B" indicates irregular borders. "C" indicates variation in colour and "D" means a diameter of more than one centimetre.

CONVERSION TABLE

In this book SI Units have been used and in parenthesis values in Metric system are given. The reader should use following instructions to convert SI Units to Metric system for the future reference.

- ❑ Urea (mmol/l) to Urea (mg/dl), multiply by 6
- ❑ Blood sugar (mmol/l) to Blood sugar (mg/dl), multiply by 18
- ❑ Creatinine (umol/l) to Creatinine (mg/dl), multiply by 0.0113
- ❑ Calcium (mmol/l) to Calcium (mg/dl), multiply by 4
- ❑ Bilirubin (umol/l) to Bilirubin (mg/dl), divide by 17.

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